PTO 1542
(4 85)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

ONLINE SEARCH REQUEST FORM

****

USER ZISKA SERIAL NUMBER 432 069

ART UNIT 154 PHONE 4495 DATE June 18, 1990

Please give a detailed statement of requirements. Describe as specifically as possible the subject matter to be searched. Define any terms that may have special meaning. Give examples or relevant citations, authors, or keywords, if known.

You may include a copy of the broadest and or relevant claim(s).

1) double cross over homologous recombination

2) production of proteins using homologous recombination

3) amplifiable gene insertion next to a target gene

4) transfer of amplifiable-target gene combo into a host

5) use of amplifiable gene to amplify target gene

Inventors

Arthur Skuntchi

Databases

CAS
Dialog
Biosis
Medline
any other applic

****

STAFF USE ONLY

COMPLETED June 25, 1990
SEARCHER Sheppard
ONLINE TIME 20 (in minutes) TOTAL TIME 30 11
NO. OF DATABASES 19

SYSTEMS
✓ CAS ONLINE
___ DARC/QUESTEL
✓ DIALOG
___ SDC
___ OTHER

Ziska
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?b biotech,155 not 42
>>>File 130 does not exist
>>>         129 does not exist
       25jun90 09:25:15 User209196 Session B94.3

System:OS  - DIALOG OneSearch

    File   5:BIOSIS PREVIEWS_69-90/MAY BA9002;RRM3902
             (C.BIOSIS 1990)

    File  10:AGRICOLA _ 1979-90/JUN
             See File 110(thru 1978)
*** AGRICOLA USERS CONFERENCE ON ALF BULLETIN BOARD, 301/344-8510, ***
***                        1200-2400 BTS,N,8,1                      ***

    File  50:CAB ABSTRACTS _ 1984-90/JUN
             SEE ALSO FILE 53 (1972-1983)
           COPR. CABI 1990.

    File  53:CAB ABSTRACTS 1972-1983
                SEE FILE 50 (1984+)
             COPR. CABI 1989

    File  72:EMBASE (EXCERPTA MEDICA)_82-90/ISS25
             (COPR. ESP BV/EM 1990)

    File 172:EMBASE (ExcerpTa Medica) 1980-81
             (Copr. ESP BV/EM 1984)

    File 173:EMBASE (ExcerpTa Medica) 1974-79
             (Copr. ESP BV/EM 1984)

    File  76:LIFE SCIENCES COLLECTION -78-90/MAR
             (Copr. Cambridge Scientific Abs.)

    File 144:PASCAL_1983 - 1990 MAR
             (C. INIST/CNRS 1990)

    File 158:DIOGENES _ 1976 - JUNE 18, 1990
             COPR. DIOGENES 1990

    File 238:SUPERTECH _ 1973-1990/MAY
             (COPR. R. R. BOWKER COMPANY 1990)
** With the UD=9001 update, subfiles TELEGEN and
   TELECOMMUNICATIONS will no longer be updated  **

   Use acronym EIC for Bowker documents through
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    File 285:BIOBUSINESS _ 1985-1990/JUL WEEK 2
           . (COPR.1990 BIOSIS)
** File 285 is now being updated 4 times a month, with weekly       **
** update codes, e.g., UD=8801W1, as well as monthly update codes, **
** e.g., UD=8801.  SDI's will continue to run monthly.              **

    File 286:BIOCOMMERCE ABS & DIRECTORY_81-90/JUN 04
             (COPR.BIOCOMMERCE  1990)
PRICE CHANGE in effect. See ?RATES.
Formats 8 ($1.50) and 9 ($2.00) for company records ONLY.
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File 55:BIOTECHNOLOGY ABSTRACTS 1982-1990/Jun
(COPR. 1990 DERWENT PUB. LTD.)

File 358:CURRENT BIOTECHNOLOGY ABS 1983-90/Jun
(COPR. 1990 ROYAL SOC CHEM)

File 581:AGRIBUSINESS U.S.A. 85-90/Jun 15
Copr. 1990 Pioneer Hi-Bred Int Inc)
** For updates prior to 11/87, use 1972 SIC Codes for SC= **
** otherwise use 1987 SIC Codes for SC=. **

File 155:MEDLINE 66-90/AUG (9008W2)

Set	Items	Description

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?s homolog?(w)recombin?
Processing
          188744  HOMOLOG?
          177966  RECOMBIN?
      S1    2671  HOMOLOG?(W)RECOMBIN?
?s s1 and crossover
            2671  S1
           22882  CROSSOVER
      S2      57  S1 AND CROSSOVER
?s s2 and double(w)crossover
              57  S2
          284825  DOUBLE
           22882  CROSSOVER
             225  DOUBLE(W)CROSSOVER
      S3      19  S2 AND DOUBLE(W)CROSSOVER
?t s3/3/1-19

 3/3/1      (Item 1 from file: 5)
0018752358      BIOSIS Number: 86124144
  HOMOLOGOUS RECOMBINATION CAN RESTORE NORMAL IMMUNOGLOBULIN PRODUCTION IN
A MUTANT HYBRIDOMA CELL LINE
  BAKER M D; PENNELL N; BOSNOYAN L; SHULMAN M J
  DEP. IMMUNOL., UNIV. TORONTO, TORONTO, ONTARIO, CANADA M5S 1A8.
  PROC NATL ACAD SCI U S A   85 (17). 1988.  6432-6436.   CODEN: PNASA
  Language: ENGLISH

 3/3/2      (Item 2 from file: 5)
0018144105      BIOSIS Number: 85067757
  ISOLATION OF AUXOTROPHIC MUTANTS OF METHYLOPHILUS-METHYLOTROPHUS BY
MODIFIED-MARKER EXCHANGE
  BOHANON M J; BASTIEN C A; YOSHIDA R; HANSON R S
  GRAY FRESHWATER BIOL. INST., UNIV. MINN., NAVARRE, MINN. 55392.
  APPL ENVIRON MICROBIOL   54 (1). 1988.  271-273.   CODEN: AEMID
  Language: ENGLISH

 3/3/3      (Item 3 from file: 5)
0015606176      BIOSIS Number: 80051174
  STRUCTURE AND BIOLOGICAL ACTIVITY OF HUMAN HOMOLOGUES OF THE RAF-MIL
ONCOGENE
  BONNER T I; KERBY S B; SUTRAVE P; GUNNELL M A; MARK G; RAPP U R
  LABORAOTRY OF CELL BIOLOGY, NATIONAL INSTITUTE OF MENTAL HEALTH,
BETHESDA, MD. 20205.
  MOL CELL BIOL   5 (6). 1985.  1400-1407.   CODEN: MCEBD
  Language: ENGLISH

 3/3/4      (Item 4 from file: 5)
0014282418      BIOSIS Number: 78018898
  LOCALIZED MUTAGENESIS IN RHIZOBIUM-JAPONICUM
  HAHN M; HENNECKE H
  MIKROBIOL. INST., EIDGENOSSISCHE TECHNISCHE HOCHSCHULE, ETH-ZENTRUM,
CH-8092 ZURICH, SWITZ.
  MOL GEN GENET   177 (1). 1984.  44-52.   CODEN: MGGEA
```

Language: ENGLISH

3/3/5 . (Item 1 from file: 50)
0306240 OS048-04734
Molecular construction and characterization of nif mutants of the obligate methanotroph Methylosinus sp. strain 6.
Toukdarian, A. E.; Lidstrom, M. E.
Department of Microbiology and Immunology, University of Washington, Seattle, Washington 98195, USA.
Journal of Bacteriology 1984. 157 (3): 979-983 (23 ref., 3 fig., 2 tab.)
Language: English

3/3/6 (Item 2 from file: 50)
0144020 OS047-00940
Localized mutagenesis in Rhizobium japonicum.
Hahn, M.; Hennecke, H.
Mikrobiologisches Institut, Eidgenossische Technische Hochschule, ETH-Zentrum, CH-8092 Zurich, Switzerland.
Molecular & General Genetics 1984. 193 (1): 46-52 (33 ref., 5 fig., 1 tab.)
Language: English

3/3/7 (Item 1 from file: 72)
07219023 EMBASE No: 88219177
Homologous recombination can restore normal immunoglobulin production in a mutant hybridoma cell line
Baker M.D.; Pennell N.; Bosnoyan L.; Shulman M.J.
Department of Immunology, University of Toronto, Toronto, Ont. M5S 1A8 Canada
PROC. NATL ACAD. SCI. U. S. A. (USA) , 1988, 85/17 (6432-6436) CODEN: PNASA ISSN: 0027-8424

3/3/8 (Item 2 from file: 72)
5895364 EMBASE No: 85140874
Structure and biological activity of human homologs of the raf/mil oncogene
Bonner T.I.; Kerby S.B.; Sutrave P.; et al.
Laboratory of Cell Biology, National Institute of Mental Health, Bethesda, MD 20205 USA
MOL. CELL. BIOL. (USA) , 1985, 5/6 (1400-1407) CODEN: MCEBD

3/3/9 (Item 3 from file: 72)
5583754 EMBASE No: 84079420
Molcular construction and characterization of nif mutants of the obligate methanotroph Methylosinus sp. strain 6
Toukdarian A.E.; Lidstrom M.E.
Department of Microbiology and Immunology, University of Washington, Seattle, WA 98195 USA
J. BACTERIOL. (USA) , 1984, 157/3 (979-983) CODEN: JOBAA

3/3/10 (Item 1 from file: 76)
1277051 82001845187
Isolation of auxotrophic mutants of Methylophilus methylotrophus by modified-marker exchange.
Bohanon, M.J.; Bastien, C.A.; Yoshida, R.; Hanson, R.S.
Gray Freshwater Biol. Inst., Univ. Minnesota, Navarre, MN 55392, USA
APPL. ENVIRON. MICROBIOL.; 54(1), pp. 271-273 1988
Language: English Summary Language: English

3/3/11 (Item 2 from file: 76)
0956851 82000994480
Structure and biological activity of human homologs of the raf/mil oncogene.
Bonner, T.I.; Kerby, S.B.; Sutrave, P.; Gunnell, M.A.; Mark, G.; Rapp,

Lab. Cell Biol., Natl. Inst. Mental Health, Bethesda, MD 20205, USA
MOL. CELL. BIOL.; 5(6), pp. 1400-1407 1985
Language: English Summary Language: English

3/3/12 (Item 3 from file: 76)
0828322 82000683992
Molecular construction and characterization of nif mutants of the obligate methanotroph Methylosinus sp. strain 6.
Toukdarian, A.E.; Lidstrom, M.E.
Dep. Microbiol. and Immunol., Univ. Washington, Seattle, WA 98195, USA
J. BACTERIOL.; 157(3), pp. 979-983 1984
Language: English Summary Language: English

3/3/13 (Item 1 from file: 357)
072863 DBA Accession No.: 88-03712
Isolation of auxotrophic mutants of Methylophilus methylotrophus by modified-marker exchange - stabilization of transposon Tn5
AUTHOR: Bohanon M J; Bastien C A; Yoshida R; +Hanson R S
CORPORATE SOURCE: Gray Freshwater Biological Institute, Univeristy of Minnesota, Navarre, Minnesota 55392, USA.
JOURNAL: Appl.Environ.Microbiol. (54, 1, 271-73) CODEN: AEMIDF
PUBLICATION YEAR: 1988 LANGUAGE: English

3/3/14 (Item 2 from file: 357)
026653 DBA Accession No.: 84-09928
Deletion of an essential gene in Escherichia coli by site-specific recombination with linear DNA fragments - studied using the alanyl-tRNA-synthetase gene
AUTHOR: Jasin M; +Schimmel P
CORPORATE SOURCE: Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA.
JOURNAL: J.Bacteriol. (159, 2, 783-86) CODEN: JOBAAY
PUBLICATION YEAR: 1984 LANGUAGE: English

3/3/15 (Item 3 from file: 357)
020908 DBA Accession No.: 84-04183
Localized mutagenesis in Rhizobium japonicum - nodulation and nitrogen-fixation analysis
AUTHOR: Hahn M; +Hennecke H
CORPORATE SOURCE: Mikrobiologisches Institut, Eidgenoessische Technische Hochschule, ETH-Zentrum, CH-8092 Zuerich, Switzerland.
JOURNAL: Mol.Gen.Genet. (193, 1, 46-52) CODEN: MGGEAE
PUBLICATION YEAR: 1984 LANGUAGE: English

3/3/16 (Item 4 from file: 357)
020691 DBA Accession No.: 84-03966
Molecular construction and characterization of nif mutants of the obligate methanotroph Methylosinus sp. strain 6 - 1-step marker-exchange procedure for transposon Tn5 mutagenesis
AUTHOR: Toukdarian A E; +Lidstrom M E
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Washington, Seattle, Washington 98195, USA.
JOURNAL: J.Bacteriol. (157, 3, 979-83) CODEN: JOBAAY
PUBLICATION YEAR: 1984 LANGUAGE: English

3/3/17 (Item 1 from file: 155)
06675454 88320454
Homologous recombination can restore normal immunoglobulin production in a mutant hybridoma cell line.
Baker MD; Pennell N; Bosnoyan L; Shulman MJ
Department of Immunology, University of Toronto, ON, Canada.
Proc Natl Acad Sci U S A Sep 1988, 85 (17) p6432-6, ISSN 0027-8424
Journal Code: PV3

3/3/18 (Item 2 from file: 155)

Structure and biological activity of human homologs of the raf/mil oncogene.
Bonner.TI; Kerby SB; Sutrave P; Gunnell MA; Mark G; Rapp UR
Laboratory of Cell Biology, National Institute of Mental Health, Bethesda, Maryland 20205.
Mol Cell Biol Jun 1985, 5 (6) p1400-7, ISSN 0270-7306
Journal Code: NGY

3/3/19 (Item 3 from file: 155)
05211617 84135617
Molecular construction and characterization of nif mutants of the obligate methanotroph Methylosinus sp. strain 6.
Toukdarian AE; Lidstrom ME
J Bacteriol Mar 1984, 157 (3) p979-83, ISSN 0021-9193
Journal Code: HH3
Contract/Grant No.: GM 07270
?s s1 and protein?
Processing
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2671 S1
1964933 PROTEIN?
S4 643 S1 AND PROTEIN?
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2923730 PRODUC?
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643 S4
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2034830 PRODUCT?
23756 PROTEIN(2N)PRODUCT?
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>>>Duplicate detection is not supported for File 158.
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S7 17 RD (unique items)
?t s7/3/1-17

7/3/1 (Item 1 from file: 5)
0020176733 BIOSIS Number: 88088923
INVOLVEMENT OF PSEUDOMONAS-PUTIDA RPON SIGMA FACTOR IN REGULATION OF VARIOUS METABOLIC FUNCTIONS
KOHLER T; HARAYAMA S; RAMOS J-L; TIMMIS K N
DEP. MED. BIOCHEM., UNIV. GENEVA, 1, RUE MICHEL-SERVET, 1211 GENEVA 4, SWITZERLAND.
J BACTERIOL 171 (8). 1989. 4326-4333. CODEN: JOBAA
Language: ENGLISH

7/3/2 (Item 2 from file: 5)

CLONING AND EXPRESSION IN ESCHERICHIA-COLI OF A REC-A-LIKE GENE FROM BACTEROIDES-FRAGILIS
GOODMAN H J K; PARKER J R; SOUTHERN J A; WOODS D R
DEP. MICROBIOL., UNIV. CAPE TOWN, RONDEBOSCH 7700, S. AFR.
GENE (AMST) 58 (2-3). 1987. 265-272. CODEN: GENED
Language: ENGLISH

7/3/3 (Item 3 from file: 5)
0017177092 BIOSIS Number: 83085216
PROTEASE-DEFICIENT BACILLUS-SUBTILIS HOST STRAINS FOR PRODUCTION OF STAPHYLOCOCCAL PROTEIN A
FAHNESTOCK S R; FISHER K E
GENEX CORPORATION, GAITHERSBURG, MARYLAND 20877.
APPL ENVIRON MICROBIOL 53 (2). 1987. 379-384. CODEN: AEMID
Language: ENGLISH

7/3/4 (Item 4 from file: 5)
0015643753 BIOSIS Number: 80067346
TRANS-ACTING AND CIS-ACTING ELEMENTS FOR THE REPLICATION OF P-1 MINIPLASMIDS
AUSTIN S J; MURAL R J; CHATTORAJ D K; ABELES A L
LABORATORY OF GENETICS AND RECOMBINANT DNA, NCI-FREDERICK CANCER RESEARCH PROGRAM, LBI-BASIC RESEARCH PROGRAM, PO BOX B, FREDERICK, MD. 21701, USA.
J MOL BIOL 183 (2). 1985. 195-202. CODEN: JMOBA
Language: ENGLISH

7/3/5 (Item 5 from file: 5)
0012274043 BIOSIS Number: 74046523
OVER PRODUCTION OF THE TRANSPOSON TN-3 TRANSPOSITION PROTEIN AND ITS ROLE IN DNA TRANSPOSITION
CASADABAN M J; CHOU J; COHEN S N
DEP. BIOPHYSICS THEORETICAL BIOL., UNIV. CHICAGO, CHICAGO, IL. 60637.
CELL 28 (2). 1982. 345-354. CODEN: CELLB
Language: ENGLISH

7/3/6 (Item 6 from file: 5)
0008165435 BIOSIS Number: 65052435
PROTEIN X IS THE PRODUCT OF THE RECA GENE OF ESCHERICHIA-COLI
MCENTEE K
DEP. BIOCHEM., STANFORD UNIV. SCH. MED., STANFORD, CALIF. 94305, USA.
PROC NATL ACAD SCI U S A 74 (12). 1977 (RECD 1978) 5275-5279. CODEN: PNASA
Language: ENGLISH

7/3/7 (Item 1 from file: 50)
0663801 OP058-01999; 6T005-02907
Induction of recombination between homoeologous chromosomes of wheat and rye.
[Abstract].
Koebner, R. M. D.; Shepherd, K. W.
Pl. Breed. Inst., Maris Lane, Trumpington, Cambridge CB2 2LQ, UK.
Heredity 1987. 59 (2): 314-315
Language: English

7/3/8 (Item 1 from file: 72)
07711735 EMBASE No: 90142170
Evidence for the double-strand break repair model of bacteriophage lambda recombination
Takahashi N.; Kobayashi I.
Department of Infectious Diseases Research, National Children's Medical Research Center, Tokyo 154 Japan
PROC. NATL. ACAD. SCI. U. S. A. (USA), 1990, 87/7 (2790-2794) CODEN: PNASA ISSN: 0027-8424

7/3/9 (Item 2 from file: 72)

Overproduction of the Tn3 transposition protein and its role in DNA transposition
Casadaban M.J.; Chou J.; Cohen S.N.
Dep. Genet., Stanford Univ., Stanford, CA 94305 USA
CELL (USA) , 1982, 28/2 (345-354) CODEN: CELLB

7/3/10 (Item 1 from file: 172)
81106621
Organization of the endogenous proviruses of chickens: Implications for origin and expression
Hughes S.H.; Toyoshima K.; Bishop J.M.; Varmus H.E.
Dept. Microbiol. Immunol., Univ. California, San Francisco, Calif. 94143 U.S.A.
VIROLOGY (U.S.A.) ,1981, 108/1 (189-207), Coden: VIRLA

7/3/11 (Item 1 from file: 144)
05929487 PASCAL No.: 85-0114758
Characterization of two strains of avian sarcoma virus isolated from avian lymphatic leukosis virus-induced sarcomas
HAGINO-YAMAGISHI K; IKAWA S; KAWAI S; HIHARA H; YAMAMOTO T; TOYOSHIMA K
Univ. Tokyo, inst. medical sci., Minato-ku Tokyo, Japan
Virology, 1984, 137 (2) 266-275
Language: English

7/3/12 (Item 1 from file: 357)
097742 DBA Accession No.: 90-00433
Expression and characterization of the Ha-ras p21 protein produced at high levels in the insect/baculo virus system - vector plasmid p36C construction by oligonucleotide site-directed mutagenesis of plasmid pAc360; application in oncogene Ha-ras p21 protein production in Spodoptera frugiperda insect cell culture
AUTHOR: Page M J; Hall A; Rhodes S; Skinner R H; Murphy V; Sydenham M
CORPORATE SOURCE: Department of Molecular Biology, Wellcome Biotech, The Wellcome Foundation, Langley Court, Beckenham, Kent BR3 3BS, UK.
JOURNAL: J.Biol.Chem. (264, 32, 19147-54) CODEN: JBCHA3
PUBLICATION YEAR: 1989 LANGUAGE: English

7/3/13 (Item 2 from file: 357)
085726 DBA Accession No.: 89-03717 PATENT
New Saccharomyces strains produced using integrating vector - inserted at a cryptic gene site and having flanking sequences of host DNA; construction of strains producing alpha-galactosidase useful in baking
PATENT ASSIGNEE: Soc.Ind.Lesaffre
PATENT NUMBER: FR 2615527 PATENT DATE: 881125 WPI ACCESSION NO.: 89-017517 (8903)
PRIORITY APPLIC. NO.: FR 877225 APPLIC. DATE: 870522
NATIONAL APPLIC. NO.: FR 877225 APPLIC. DATE: 870522
PUBLICATION YEAR: 1988 LANGUAGE: French

7/3/14 (Item 3 from file: 357)
084571 DBA Accession No.: 89-02562 PATENT
Raccoon pox virus, rabies virus recombinant protein production - for use in disease diagnosis or vaccine production
PATENT ASSIGNEE: U.S.Dept.Health-Human-Serv.
PATENT NUMBER: US 7198213 PATENT DATE: 881101 WPI ACCESSION NO.: 88-360972 (8850)
PRIORITY APPLIC. NO.: US 198213 APPLIC. DATE: 880525
NATIONAL APPLIC. NO.: US 198213 APPLIC. DATE: 880525
PUBLICATION YEAR: 1988 LANGUAGE: English

7/3/15 (Item 4 from file: 357)
081856 DBA Accession No.: 88-12705
New genetic methods for mammalian cells - including nonsense suppression, controlled amplification and gene targeting by homologous recombination
AUTHOR: Sedivy J M

CORPORATE SOURCE: Department of Molecular Biophysics and Biochemistry, Yale University School of Medicine, 333 Cedar Street, New Haven, Connecticut 06510, USA.
JOURNAL: Bio/Technology (6, 10, 1192-96) CODEN: BTCHDA
PUBLICATION YEAR: 1988 LANGUAGE: English

7/3/16 (Item 5 from file: 357)
063439 DBA Accession No.: 87-07787
Vaccinia virus recombinants expressing the SA11 rota virus VP7 glycoprotein gene induce serotype-specific neutralizing antibodies - application for rota virus vaccine development
AUTHOR: Andrew M E; Boyle D B; Coupar B E H; Whitfeld P L; Both G W; +Bellamy A R
CORPORATE SOURCE: Department of Cell Biology, University of Auckland, Auckland, New Zealand.
JOURNAL: J.Virol. (61, 4, 1054-60) CODEN: JOVIAM
PUBLICATION YEAR: 1987 LANGUAGE: English

7/3/17 (Item 1 from file: 155)
05621520 85237520
Trans- and cis-acting elements for the replication of P1 miniplasmids.
Austin SJ; Mural RJ; Chattoraj DK; Abeles AL
NCI-Frederick Cancer Research Program, Md 21701.
J Mol Biol May 25 1985, 183 (2) p195-202, ISSN 0022-2836
Journal Code: J6V
Contract/Grant No.: NO1-CO-23909
?s gene?(n)amplifi?
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4067996 GENE?
44339 AMPLIFI?
S8 9464 GENE?(N)AMPLIFI?
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Processing
9464 S8
126027 INSERT?
S9 599 S8 AND INSERT?
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130081 TARGET
599 S9
S10 34 TARGET AND S9
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>>>Duplicate detection is not supported for File 158.
>>>Duplicate detection is not supported for File 286.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
S11 27 RD (unique items)
?t s11/3/1-27

11/3/1 (Item 1 from file: 5)
0020863515 BIOSIS Number: 89045924
GENE AMPLIFICATION CONTRIBUTES TO SULFONAMIDE RESISTANCE IN ESCHERICHIA-COLI
NICHOLS B P; GUAY G G
LAB. CELL MOLECULAR DEV. BIOL., DEP. BIOL. SCI., UNIV. ILL. AT CHICAGO, P.O. BOX 4348, CHICAGO, ILL. 60680.
ANTIMICROB AGENTS CHEMOTHER 33 (12). 1989. 2042-2048. CODEN: AMACC
Language: ENGLISH

11/3/2 (Item 2 from file: 5)
0016094500 BIOSIS Number: 81042774
A PBR-322-DERIVED VECTOR FOR CLONING BLUNT-ENDED COMPLEMENTARY DNA ITS USE TO DETECT MOLECULAR CLONES OF LOW-ABUNDANCE MESSENGER RNA SPECIES
EDWARDS D R; PARFETT C L J; DENHARDT D T
CANCER RESEARCH LABORATORY, UNIVERSITY OF WESTERN ONTARIO, LONDON, ONTARIO, CANADA N6A 5B7.
DNA (N Y) 4 (5). 1985. 401-408. CODEN: DNAAD
Language: ENGLISH

11/3/3 (Item 1 from file: 72)
07489998 EMBASE No: 89212810
Rapid, nonradioactive detection of mutations in the human genome by allele-specific amplification
Okayama H.; Curiel D.T.; Brantly M.L.; Holmes M.D.; Crystal D.G.
Pulmonary Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD 20892 USA
J. LAB. CLIN. MED. (USA) , 1989, 114/2 (105-113) CODEN: JLCMA ISSN: 0022-2143

11/3/4 (Item 2 from file: 72)
07345224 EMBASE No: 89061518
Transcription-based amplification system and detection of amplified human immunodeficiency virus type 1 with a bead-based sandwich hybridization format
Kwoh D.Y.; Davis G.R.; Whitfield K.M.; Chappelle H.L.; DiMichelle L.J.; Gingeras T.R.
SISKA Diagnostics and The Salk Institute Biotechnology/Industrial Associates, Inc., La Jolla, CA 92037 USA
PROC. NATL ACAD. SCI. U. S. A. (USA) , 1989, 86/4 (1173-1177) CODEN: PNASA ISSN: 0027-8424

11/3/5 (Item 1 from file: 76)
260431 79062105188
Cloning and amplification of DNA sequences encoding a trimethoprim-resistant dihydrofolate reductase gene.;
Fling,M. ; Elwell,L.P. ; Inamine,J.M.
(Wellcome Res. Lab., Research Triangle Park, NC 27709, USA)
Publ: Publ. by: Elsevier/North-Holland Biomedical Press, 335 Jan van Galenstraat, PO Box 211, Amsterdam, Netherlands. 1978 p. 173-180 1978
In: Genetic engineering. Boyer,H.W.; Nicosia,S. (eds.)
0-444-80065-4;
Language: English; Summary Language: English

11/3/6 (Item 1 from file: 357)
080247 DBA Accession No.: 88-11096
Rapid production of vector-free biotinylated probes using the polymerase chain reaction - construction of amplified biotin-labeled DNA probe
AUTHOR: Lo Y M D; Mehal W Z; Fleming K A
CORPORATE SOURCE: University of Oxford, Nuffield Department of Pathology, John Radcliffe Hospital, Oxford, OX3 9DU, UK.
JOURNAL: Nucleic Acids Res. (16, 17, 8719) CODEN: NARHAD
PUBLICATION YEAR: 1988 LANGUAGE: English

11/3/7 (Item 2 from file: 357)
028756 DBA Accession No.: 84-12031
Natural mechanisms of microbial evolution - recombinant DNA technology (conference paper)
AUTHOR: Arber W
CORPORATE SOURCE: Dept. of Microbiology, Biozentrum of the University of Basel, Klingelbergstrasse 70, CH-4056 Basel, Switzerland. (1-13)
CODEN: 9999Z
PUBLICATION YEAR: 1984 LANGUAGE: English

11/3/8 (Item 1 from file: 358)

Process for amplifying expression of cloned genes in eukaryotic cells.
AUTHOR: Bestwick, R. K.; Kabat, D.
CODEN: PIXXD2
PATENT NUMBER: WO 8808454
PATENT APPLICATION: US 041523 (870423)
COMPANY: Oregon Health Sciences University, USA
PUBLICATION DATE: 3 Nov 1988 (881103) LANGUAGE: English

11/3/9 (Item 2 from file: 358)
015003 CBA Acc. No.: 04-06-002015 DOC. TYPE: Journal
A pBR322-derived vector for cloning blunt-ended cDNA: its use to detect molecular clones of low-abundance mRNAs.
AUTHOR: Edwards, D. R.; Parfett, C. L. J.; Denhardt, D. T.
CORPORATE SOURCE: Univ. Western Ontario, Cancer Res. Lab., London, ON, N6A 5B7, Canada
JOURNAL: DNA Volume: 4 Issue: 5 Page(s): 401-408
CODEN: DNAADR ISSN: 0198-0238
PUBLICATION DATE: Oct 1985 (851000) LANGUAGE: English

11/3/10 (Item 1 from file: 155)
07278189 90185189
Precise excision of telomere-bearing transposons during Oxytricha fallax macronuclear development.
Hunter DJ; Williams K; Cartinhour S; Herrick G
Cellular, Viral, and Molecular Biology, University of Utah School of Medicine, Salt Lake City 84132.
Genes Dev (UNITED STATES) Dec 1989, 3 (12B) p2101-12, ISSN 0890-9369 Journal Code: FN3
Contract/Grant No.: GM-25203

11/3/11 (Item 2 from file: 155)
07199883 90106883
DNA base changes in benzo[a]pyrene diol epoxide-induced dihydrofolate reductase mutants of Chinese hamster ovary cells.
Carothers AM; Grunberger D
Institute of Cancer Research, Columbia University, New York, NY 10032.
Carcinogenesis (UNITED STATES) Jan 1990, 11 (1) p189-92, ISSN 0143-3334 Journal Code: C9T
Contract/Grant No.: CA39547; CA31696; CA21111

11/3/12 (Item 3 from file: 155)
07190865 90097865
cDNA genes formed after infection with retroviral vector particles lack the hallmarks of natural processed pseudogenes.
Dornburg R; Temin HM
McArdle Laboratory for Cancer Research, University of Wisconsin, Madison 53706.
Mol Cell Biol (UNITED STATES) Jan 1990, 10 (1) p68-74, ISSN 0270-7306 Journal Code: NGY
Contract/Grant No.: CA-22443; CA-07175

11/3/13 (Item 4 from file: 155)
07176275 90083275
Targeted gene mutations in Drosophila.
Ballinger DG; Benzer S
Division of Biology, California Institute of Technology, Pasadena 91125.
Proc Natl Acad Sci U S A (UNITED STATES) Dec 1989, 86 (23) p9402-6, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: GM 40499

11/3/14 (Item 5 from file: 155)
07160910 90067910
Sequence and characteristics of IS900, an insertion element identified in a human Crohn's disease isolate of Mycobacterium paratuberculosis.
Green EP; Tizard ML; Moss MT; Thompson J; Winterbourne DJ; McFadden JJ;

Department of Surgery, St Georges Hospital Medical School, London, UK.
Nucleic Acids Res (ENGLAND) Nov 25 1989, 17 (22) p9063-73, ISSN 0305-1048 Journal Code: O8L

11/3/15 (Item 6 from file: 155)
07099749 90006749
High-copy-number integration into the ribosomal DNA of Saccharomyces cerevisiae: a new vector for high-level expression.
Lopes TS; Klootwijk J; Veenstra AE; van der Aar PC; van Heerikhuizen H; Raue HA; Planta RJ
Biochemisch Laboratorium, Vrije Universiteit, Amsterdam, The Netherlands.
Gene (NETHERLANDS) Jul 15 1989, 79 (2) p199-206, ISSN 0378-1119 Journal Code: FOP

11/3/16 (Item 7 from file: 155)
07032356 89334356
Novel method for monitoring genetically engineered microorganisms in the environment.
Chaudhry GR; Toranzos GA; Bhatti AR
Institute of Food and Agricultural Sciences, University of Florida, Gainesville 32611.
Appl Environ Microbiol May 1989, 55 (5) p1301-4, ISSN 0099-2240 Journal Code: 6K6

11/3/17 (Item 8 from file: 155)
06916951 89218951
Genetic structure, function and regulation of the transposable element IS21.
Reimmann C; Moore R; Little S; Savioz A; Willetts NS; Haas D
Mikrobiologisches Institut, Eidgenossische Technische Hochschule, Zurich, Switzerland.
Mol Gen Genet Feb 1989, 215 (3) p416-24, ISSN 0026-8925 Journal Code: NGP
Contract/Grant No.: AI-12899

11/3/18 (Item 9 from file: 155)
06714573 89016573
Expression and amplification in transgenic mice of a polyoma virus mutant regulatory region.
Krippl B; Griep AE; Mahon KA; Bohnlein E; Gruss P; Westphal H
Laboratory of Molecular Genetics, National Institute of Child Health and Human Development, Bethesda, MD 20892.
Nucleic Acids Res Sep 26 1988, 16 (18) p8963-76, ISSN 0305-1048 Journal Code: O8L

11/3/19 (Item 10 from file: 155)
06303396 87277396
Reverse-transcribed pseudogenes of U1 small nuclear RNA presumably amplified in the rat genome together with the flanking region.
Watanabe-Nagasu N; Satoh H; Ohshima Y
Gene 1987, 52 (2-3) p235-43, ISSN 0378-1119 Journal Code: FOP

11/3/20 (Item 11 from file: 155)
06229362 87203362
Molecular analysis of elements inserted into mouse gamma-actin processed pseudogenes.
Man YM; Delius H; Leader DP
Nucleic Acids Res Apr 24 1987, 15 (8) p3291-304, ISSN 0305-1048 Journal Code: O8L

11/3/21 (Item 12 from file: 155)
05931614 86232614
Target sites for the transposition of rat long interspersed repeated DNA elements (LINEs) are not random.
Furano AV; Somerville CC; Tsichlis PN; D'Ambrosio E

Section on Genomic Structure and Function, National Institute of Arthritis, Bethesda, MD 20892.
Nucleic Acids Res May 12 1986, 14 (9) p3717-27, ISSN 0305-1048 Journal Code: O8L
Contract/Grant No.: CA-38047; CA-06927; RR-05539

11/3/22 (Item 13 from file: 155)
05752278 86053278
Cell culture studies on the mechanism of action of chemical carcinogens and tumor promoters.
Weinstein IB
Division of Environmental Sciences, Columbia University, New York 10032.
Carcinog Compr Surv 1985, 10 p177-87, ISSN 0147-4006 Journal Code: CNU
Contract/Grant No.: CA 021111; CA 26056

11/3/23 (Item 14 from file: 155)
05618597 85234597
Sequence rearrangements and genome instability. A possible step in carcinogenesis.
Chorazy M
Department of Tumor Biology, Institute of Oncology, Gliwice, Poland.
J Cancer Res Clin Oncol 1985, 109 (3) p159-72, ISSN 0171-5216 Journal Code: HL5
Document Type: Review

11/3/24 (Item 15 from file: 155)
05560757 85176757
Mechanisms of multistage chemical carcinogenesis and their relevance to respiratory tract cancer.
Weinstein IB; Arcoleo J; Lambert M; Hsiao W; Gattoni-Celli S; Jeffrey AM; Kirschmeier P
Division of Environmental Sciences, Columbia University, New York, New York 10032.
Carcinog Compr Surv 1985, 8 p395-409, ISSN 0147-4006 Journal Code: CNU
Contract/Grant No.: CA 021111; CA 26056

11/3/25 (Item 16 from file: 155)
05135051 84059051
Specificity of transposon Tn5 insertion.
Berg DE; Schmandt MA; Lowe JB
Genetics Dec 1983, 105 (4) p813-28, ISSN 0016-6731 Journal Code: FNH
Contract/Grant No.: AI 14267; AI 18980

11/3/26 (Item 17 from file: 155)
05112181 84036181
Two adjacent genomic zein sequences: structure, organization and tissue-specific restriction pattern.
Spena A; Viotti A; Pirrotta V
J Mol Biol Oct 5 1983, 169 (4) p799-811, ISSN 0022-2836 Journal Code: J6V

11/3/27 (Item 18 from file: 155)
04482582 82025582
Transposon-mediated site-specific recombination: a defined in vitro system.
Reed RR
Cell Sep 1981, 25 (3) p713-9, ISSN 0092-8674 Journal Code: CQ4
?Processing
Processing
9464 S8
513162 TRANSFER?
S12 576 S8 AND TRANSFER?
?s s12 and target

```
            130081  TARGET.
     S13         11  S12 AND TARGET
?s s13 not s11
                11  S13
                27  S11
     S14         10  S13 NOT S11
?# s14/3/1010
>>>Item 1010 is not within valid item range for file 155
?t s14/3/1-10

 14/3/1      (Item 1 from file: 72)
07560480   EMBASE No: 89125694
  Helpers for efficient encapsidation of SV40 pseudovirions
  Oppenheim A.; Peleg A.
  Department of Hematology, Hadassah University Hospital, Jerusalem  Israel
  GENE (Netherlands) , 1989, 77/1 (79-86)  CODEN: GENED   ISSN: 0378-1119

 14/3/2      (Item 1 from file: 172)
80135318   0250240200527
  Appearance  and  distribution  of virally determined antigens in lymphoid
organs of mice during leukemogenesis by Moloney leukemia virus
  Asjo B.; Fenyo E.M.; Spira J.; Klein G.
  Dept. Tum. Biol., Karolinska Inst., S-104 01 Stockholm 60
  SWEDEN
  LEUK. RES. (ENGLAND)   ,1980,   4/1 (89-103),  Coden: LERED

 14/3/3      (Item 1 from file: 76)
0663661  82000257069
  Organization of the Methotrexate Resistant Mouse L5178YR Dihydrofolate
Reductase Gene and Transformation of Human HCT-8 Cells by this Gene.
  Presented at: Deutsche Gesellschaft Hamatologie und Onkologie and the
Deutsche Krebsforschungszentrum, Wilsede (FRG), 16-19 Jun 1980
  Bertino, J.R.; Scheer, D.I.; Srimatkandada, S.; Kamen, B.A.; Dube, S.
  Yale Univ. Sch. Med., 333 Cedar St., New Haven, CT 06510, USA
  HAEMATOLOGY AND BLOOD TRANSFUSION; 26
  Publ: Publ by: SPRINGER-VERLAG, BERLIN (FRG), 1981, pp. 171-174  1981
  In MODERN TRENDS IN LEUKEMIA. IV. LATEST RESULTS IN CLINICAL AND
BIOLOGICAL RESEARCH INCLUDING PEDIATRIC ONCOLOGY. Neth, R.; Gallo, R.C.;
Graf, T.; Mannweiler, K.; Winkler, K. (eds.)
  Language: English

 14/3/4      (Item 1 from file: 357)
080858  DBA Accession No.: 88-11707
Recombinant fragment assay for gene targeting based on the polymerase chain
    reaction - detection of homologous recombinant DNA fragment by
    selective amplification
AUTHOR: Kim H S;  Smithies O
CORPORATE SOURCE: Laboratory of Medical Genetics and Genetics, University
    of Wisconsin, Madison, WI 53706, USA.
JOURNAL: Nucleic Acids Res.  (16, 18, 8887-903)   CODEN: NARHAD
PUBLICATION YEAR: 1988   LANGUAGE: English

 14/3/5      (Item 2 from file: 357)
047822  DBA Accession No.: 86-05670
Normal and neoplastic differentiation: programming genes, gene dosage and
    shuttle vectors - shuttle vector development (conference abstract)
AUTHOR: Bertolotti R;  Lutfalla G
CORPORATE AFFILIATE: Mol.Genetics
CORPORATE SOURCE: Molecular Genetica, Gif sur Yvette, France.
JOURNAL: J.Cell.Biochem.  (Suppl.10C, 111)   CODEN: 5210J
PUBLICATION YEAR: 1986   LANGUAGE: English

 14/3/6      (Item 1 from file: 155)
07319303   90226303
  Synthesis  in  vitro and application of biotinylated DNA probes for human
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papillomavirus type 16 by utilizing the polymerase chain reaction.
Day PJ; Bevan IS; Gurney SJ; Young LS; Walker MR
Department of Clinical Chemistry, University of Birmingham, Edgbaston, U.K.
Biochem J (ENGLAND) Apr 1 1990, 267 (1) p119-23, ISSN 0264-6021 Journal Code: 9YO

14/3/7 (Item 2 from file: 155)
07023483 89325483
A sensitive technique to monitor gene transfer and expression in bone marrow stem cells.
Narayanan R; Tare NS; Benjamin WR; Gubler U
Department of Molecular Genetics, Hoffmann-La Roche Incorporated, Nutley, New Jersey 07110.
Exp Hematol Aug 1989, 17 (7) p832-5, ISSN 0301-472X Journal Code: EPR

14/3/8 (Item 3 from file: 155)
06747131 89049131
DNA amplification to enhance detection of genetically engineered bacteria in environmental samples.
Steffan RJ; Atlas RM
Department of Biology, University of Louisville, Kentucky 40292.
Appl Environ Microbiol Sep 1988, 54 (9) p2185-91, ISSN 0099-2240 Journal Code: 6K6

14/3/9 (Item 4 from file: 155)
05514051 85130051
RSV provirus with same flanking sequences is found on different size classes of Chinese hamster chromosomes.
Hillova J; Hill M; Mariage-Samson R; Belehradek J Jr
Laboratory of Cellular and Molecular Biology, Institute of Cancerology and Immunogenetics, Villejuif, France.
Intervirology 1985, 23 (1) p29-43, ISSN 0300-5526 Journal Code: GW7

14/3/10 (Item 5 from file: 155)
05074371 83307371
Amplification of the aroA gene from Escherichia coli results in tolerance to the herbicide glyphosate.
Rogers SG; Brand LA; Holder SB; Sharps ES; Brackin MJ
Appl Environ Microbiol Jul 1983, 46 (1) p37-43, ISSN 0099-2240 Journal Code: 6K6
?ds s15-
ds s15-s16

Set	Items	Description
S15	24	E2-E6
S16	1	S15 AND S1

?t s16/3

16/3/1 (Item 1 from file: 76)
1261981 82001810159
Regulated expression of genes inserted at the human chromosomal .beta.-globin locus by homologous recombination.
Nandi, A.K.; Roginski, R.S.; Gregg, R.G.; Smithies, O.; Skoultchi, A.I.
Dep. Cell Biol., Albert Einstein Coll. Med., 1300 Morris Park Ave., Bronx, NY 10461, USA
PROC. NATL. ACAD. SCI. USA; 85(11), pp. 3845-3849 1988
Language: English Summary Language: English
?fil ca
FILE 'CA' ENTERED AT 10:55:21 ON 25 JUN 90
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FILE COVERS 1967 - 23 June 90 (900623/ED) VOL 113 ISS 2

All OFFLINE Prints or Displays, use the ABS or ALL formats
to obtain abstract graphic structures. The AB format DOES
NOT display structure diagrams.

```
=> s homolog?(w)recombina?)/ab,bi
         33462 HOMOLOG?/AB
         12506 HOMOLOG?/BI
         53388 RECOMBINA?/AB
         32966 RECOMBINA?/BI
L1         765 (HOMOLOG?(W)RECOMBINA?)/AB,BI

=> s l1 and (double(w)crossover)/ab,bi
        111955 DOUBLE/AB
         46780 DOUBLE/BI
          5004 CROSSOVER/AB
           932 CROSSOVER/BI
            36 (DOUBLE(W)CROSSOVER)/AB,BI
L2           5 L1 AND (DOUBLE(W)CROSSOVER)/AB,BI

=> d an ti so au pi ai py 1-5

L2  ANSWER 1 OF 5
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AN   CA109(19):164833u
TI   Homologous recombination can restore normal immunoglobulin
     production in a mutant hybridoma cell line
SO   Proc. Natl. Acad. Sci. U. S. A., 85(17), 6432-6
AU   Baker, Mark D.; Pennell, Nancy; Bosnoyan, Lucine; Shulman, Marc J.
PY   1988

L2  ANSWER 2 OF 5
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AN   CA105(19):166272b
TI   Recombination of homologous DNA fragments transfected into mammalian
     cells occurs predominantly by terminal pairing
SO   Mol. Cell. Biol., 6(9), 3246-52
AU   Anderson, Richard A.; Eliason, Steven L.
PY   1986

L2  ANSWER 3 OF 5
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AN   CA103(7):49032w
TI   Structure and biological activity of human homologs of the raf/mil
     oncogene
SO   Mol. Cell. Biol., 5(6), 1400-7
AU   Bonner, Tom I.; Kerby, Stephen B.; Sutrave, Pramod; Gunnell, Mark
     A.; Mark, George; Rapp, Ulf R.
PY   1985

L2  ANSWER 4 OF 5
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN   CA100(19):151818g
TI   Molecular construction and characterization of nif mutants of the
     obligate methanotroph Methylosinus sp. strain 6
SO   J. Bacteriol., 157(3), 979-83
AU   Toukdarian, Aresa E.; Lidstrom, Mary E.
PY   1984

L2  ANSWER 5 OF 5
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```

```
AN   CA100(15):115675z
TI   Localized mutagenesis in Rhizobium japonicum
SO   MGG, Mol. Gen. Genet., 193(1), 46-52
AU   Hahn, Matthias; Hennecke, Hauke
PY   1984

=> s pprobbein(1a)product?)/ab,bi
        365365 PROTEIN/AB
        281535 PROTEIN/BI
        542053 PRODUCT?/AB
        396809 PRODUCT?/BI
L3        5020 (PROTEIN(1A)PRODUCT?)/AB,BI

=> s l3 and l1
L4           5 L3 AND L1

=> d an ti so au pi ai py 1-5

L4  ANSWER 1 OF 5
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN   CA109(7):49643v
TI   Viral vectors encoding human immunodeficiency virus (HIV) F protein
     and use of these vectors for vaccination
SO   Fr. Demande, 31 pp.
AU   Kieny, Marie Paule; Guy, Bruno; Lecocq, Jean Pierre; Montagnier, Luc
PI   FR 2600079  A1  18 Dec 1987
AI   FR 86-8698  16 Jun 1986
PY   1987

L4  ANSWER 2 OF 5
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AN   CA107(15):128481c
TI   Lytic viruses as expression vectors, host cell containing same and
     process for protein production
SO   PCT Int. Appl., 27 pp.
AU   Von Gabain, Alexander Ulrich
PI   WO 8702702  A1  7 May 1987
AI   WO 86-SE477  15 Oct 1986
PY   1987

L4  ANSWER 3 OF 5
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AN   CA103(7):48861d
TI   Trans- and cis-acting elements for the replication of P1
     miniplasmids
SO   J. Mol. Biol., 183(2), 195-202
AU   Austin, Stuart J.; Mural, Richard J.; Chattoraj, Dhruba K.; Abeles,
     Ann L.
PY   1985

L4  ANSWER 4 OF 5
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AN   CA93(21):199420k
TI   Analysis of the nucleotide sequence of an invertible controlling
     element
SO   Proc. Natl. Acad. Sci. U. S. A., 77(7), 4196-200
AU   Zieg, Janine; Simon, Melvin
PY   1980

L4  ANSWER 5 OF 5
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AN    CA88(13):85860v
TI    Protein X is the product of the recA gene of Escherichia coli
SO    Proc. Natl. Acad. Sci. U. S. A., 74(12), 5275-9
AU    McEntee, Kevin
PY    1977

=> s ggeee(w)insertion)/ab,bi
         84022 GENE/AB
        109666 GENE/BI
         15912 INSERTION/AB
          9208 INSERTION/BI
L5         194 (GENE(W)INSERTION)/AB,BI

=> s l5 and l1
L6           4 L5 AND L1

=> d an ti so au pi ai py 1-4

L6  ANSWER 1 OF 4
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AN    CA109(23):206247p
TI    Construction of recombinant fowlpox virus or avian poxviruses and
      their use as vaccines against avian diseases
SO    PCT Int. Appl., 55 pp.
AU    Boyle, David Bernard; Coupar, Barbara Elizabeth Howieson; Both,
      Gerald Wayne
PI    WO 8802022  A1  24 Mar 1988
AI    WO 87-AU323  22 Sep 1987
PY    1988

L6  ANSWER 2 OF 4
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AN    CA108(24):210170e
TI    Construction of recombinant enterobacterium containing mutant galE
      gene for use as live vaccine
SO    Eur. Pat. Appl., 20 pp.
AU    Hone, David Michael; Hackett, James Anthony
PI    EP 249449  A1  16 Dec 1987
AI    EP 87-305108  10 Jun 1987
PY    1987

L6  ANSWER 3 OF 4
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AN    CA107(5):34257g
TI    Disruption of the Dictyostelium myosin heavy chain gene by
      homologous recombination
SO    Science (Washington, D. C., 1883-), 236(4805), 1086-91
AU    De Lozanne, Arturo; Spudich, James A.
PY    1987

L6  ANSWER 4 OF 4
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AN    CA105(17):147531u
TI    Shuttle mutagenesis:  a method of introducing transposons into
      transformable organisms
SO    Genet. Eng. (N. Y.), 8, 123-33
AU    Seifert, H. Steven; So, Magdalene; Heffron, Fred
PY    1986

=> transfer?/ab,bi
        248336 TRANSFER?/AB
```

```
L7        321541 TRANSFER?/AB,BI

=> s gene(a)amplifi?)/ab,bi
          84022 GENE/AB
         109666 GENE/BI
          19745 AMPLIFI?/AB
           8505 AMPLIFI?/BI
L8          1272 (GENE(A)AMPLIFI?)/AB,BI

=> s target/ab,bi
          51727 TARGET/AB
          14302 TARGET/BI
L9             43 L8 AND TARGET/AB,BI

=> s l9 and insert?/ab,bio
          41474 INSERT?/AB
          11862 INSERT?/BI
L10             2 L9 AND INSERT?/AB,BI

=> d 1-2

L10 ANSWER 1 OF 2
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AN   CA112(7):49603u
TI   Gene amplification contributes to sulfonamide resistance in
     Escherichia coli
AU   Nichols, Brian P.; Guay, Gordon G.
CS   Dep. Biol. Sci., Univ. Illinois
LO   Chicago, IL 60680, USA
SO   Antimicrob. Agents Chemother., 33(12), 2042-8
SC   3-2 (Biochemical Genetics)
DT   J
CO   AMACCQ
IS   0066-4804
PY   1989
LA   Eng

L10 ANSWER 2 OF 2
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AN   CA109(25):223667t
TI   Molecular basis of genome rearrangements at the hamster aprt locus
AU   Meuth, Mark; Nalbantoglu, Josephine; Phear, Geraldine; Miles, Carol
CS   Clare Hall Lab., Imp. Cancer Res. Fund
LO   South Mimms/Hertfordshire EN6 3LD, UK
SO   Banbury Rep., 28(Mamm. Cell Mutagen.), 183-91
SC   3-3 (Biochemical Genetics)
SX   13
DT   J
CO   BANRDU
IS   0198-0068
PY   1987
LA   Eng

=>
L11             3 L9 AND L7

=> d 1-2

L11 ANSWER 1 OF 3
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AN   CA111(7):51682s
TI   Hybrid DNA artifact from PCR of closely related target sequences
AU   Shuldiner, Alan R.; Nirula, Ajay; Roth, Jess
```

CS Diabetes Branch, NIDDK
LO Bethesda, MD 20892, USA
SO Nucleic Acids Res., 17(11), 4409
SC 3-5 (Biochemical Genetics)
DT J
CO NARHAD
IS 0305-1048
PY 1989
LA Eng

L11 ANSWER 2 OF 3
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AN CA109(25):223667t
TI Molecular basis of genome rearrangements at the hamster aprt locus
AU Meuth, Mark; Nalbantoglu, Josephine; Phear, Geraldine; Miles, Carol
CS Clare Hall Lab., Imp. Cancer Res. Fund
LO South Mimms/Hertfordshire EN6 3LD, UK
SO Banbury Rep., 28(Mamm. Cell Mutagen.), 183-91
SC 3-3 (Biochemical Genetics)
SX 13
DT J
CO BANRDU
IS 0198-0068
PY 1987
LA Eng

=> d 3

L11 ANSWER 3 OF 3
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AN CA106(25):211581k
TI Amplification of dihydrofolate reductase genes and their transfer to animal cells
AU Kuznetsova, N. N.; Mukhamedkhanova, F. S.; Nuridzhanyants, S. S.; Abdukarimov, A. A.; Sadykov, A. S.
CS Inst. Bioorg. Chem.
LO Tashkent, USSR
SO Biopolim. Kletka, 3(2), 88-95, 2 plates
SC 13-4 (Mammalian Biochemistry)
SX 3
DT J
CO BIKLEK
PY 1987
LA Russ

=> s l9 not (l2 or l4 or l6 or l10 or l11)
L12   39 L9 NOT (L2 OR L4 OR L6 OR L10 OR L11)

=> s l12 and l1
L13   0 L12 AND L1

=> d an ti so au pi ai py 1-39
'L13' HAS NO ANSWERS
L1   765 SEA (HOMOLOG?(W)RECOMBINA?)/AB,BI
L2   5 SEA L1 AND (DOUBLE(W)CROSSOVER)/AB,BI
L3   5020 SEA (PROTEIN(1A)PRODUCT?)/AB,BI
L4   5 SEA L3 AND L1
L5   194 SEA (GENE(W)INSERTION)/AB,BI
L6   4 SEA L5 AND L1
L7   321541 SEA TRANSFER?/AB,BI
L8   1272 SEA (GENE(A)AMPLIFI?)/AB,BI
L9   43 SEA L8 AND TARGET/AB,BI
L10   2 SEA L9 AND INSERT?/AB,BI

L11 3 SEA L7 AND L
L12 39 SEA L9 NOT (L2 OR L4 OR L6 OR L10 OR L11)
L13 0 SEA L12 AND L1

=> d l12 an ti so au pi ai py 1-39

L12 ANSWER 1 OF 39
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AN CA112(25):230770m
TI A method for difference cloning: gene amplification following subtractive hybridization
SO Proc. Natl. Acad. Sci. U. S. A., 87(7), 2720-4
AU Wieland, Ilse; Bolger, Graeme; Asouline, Gigi; Wigler, Michael
PY 1990

L12 ANSWER 2 OF 39
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AN CA112(19):174984v
TI Direct and sensitive detection of a pathogenic protozoan, Toxoplasma gondii, by polymerase chain reaction
SO J. Clin. Microbiol., 27(8), 1787-92
AU Burg, J. Lawrence; Grover, Christopher M.; Pouletty, Philippe; Boothroyd, John C.
PY 1989

L12 ANSWER 3 OF 39
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AN CA112(15):133790k
TI Single primer pair for amplifying segments of distinct Shiga-like-toxin genes by polymerase chain reaction
SO J. Clin. Microbiol., 27(12), 2751-7
AU Karch, Helge; Meyer, Thomas
PY 1989

L12 ANSWER 4 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA112(3):17342s
TI Rapid determination of bacterial ribosomal RNA sequences by direct sequencing of enzymically amplified DNA
SO FEMS Microbiol. Lett., 65(1-2), 171-6
AU Boettger, Erik C.
PY 1989

L12 ANSWER 5 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA112(1):1995w
TI Detection of amplified oncogenes by differential polymerase chain reaction
SO Oncogene, 4(9), 1153-7
AU Frye, Roy A.; Benz, Christopher C.; Liu, Edison
PY 1989

L12 ANSWER 6 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA111(25):226299b
TI Analysis of ras gene mutations and methylation state in human leukemias
SO Oncogene, 4(8), 1029-36
AU Browett, Peter J.; Norton, John D.
PY 1989

L12 ANSWER 7 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA111(17):147625b
TI A subset of herpes simplex virus replication genes induces DNA amplification within the host cell genome
SO J. Virol., 63(9), 3683-92
AU Heilbronn, Regine; Zur Hausen, Harald
PY 1989

L12 ANSWER 8 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA111(7):51668s
TI Direct detection of point mutations by mismatch analysis: application to hemophilia B
SO Nucleic Acids Res., 17(9), 3347-58
AU Montandon, A. J.; Green, P. M.; Giannelli, F.; Bentley, D. R.
PY 1989

L12 ANSWER 9 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA111(3):18837y
TI Gene amplification with immobilized primer
SO Eur. Pat. Appl., 7 pp.
AU Dattagupta, Nanibhushan
PI EP 297379 A2 4 Jan 1989
AI EP 88-109769 20 Jun 1988
PY 1989

L12 ANSWER 10 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA111(3):18784d
TI Helpers for efficient encapsidation of SV40 pseudovirions
SO Gene, 77(1), 79-86
AU Oppenheim, Ariella; Peleg, Aviva
PY 1989

L12 ANSWER 11 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA110(21):188623x
TI Enzymic gene amplification: qualitative and quantitative methods for detecting proviral DNA amplified in vitro
SO J. Infect. Dis., 158(6), 1158-69
AU Abbott, Mark A.; Poiesz, Bernard J.; Byrne, Bruce C.; Kwok, Shirley; Sninsky, John J.; Ehrlich, Garth D.
PY 1988

L12 ANSWER 12 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA110(19):167215a
TI Amplification of a polymorphic dihydrofolate reductase gene expressing an enzyme with decreased binding to methotrexate in a human colon carcinoma cell line, HCT-8R4, resistant to this drug
SO J. Biol. Chem., 264(6), 3524-8
AU Srimatkandada, Srinivasan; Schweitzer, Barry I.; Moroson, Barbara A.; Dube, Shyam; Bertino, Joseph R.
PY 1989

L12 ANSWER 13 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA109(23):206006j
TI Somatic cell genetic studies of amplificator cell lines
SO Cancer Cells, 6(Eukaryotic DNA Replication), 325-8
AU Rolfe, M.; Knights, C.; Stark, G. R.
PY 1988

L12 ANSWER 14 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA109(19):168196m
TI Amplification of epidermal growth factor receptor gene but no evidence of ras mutations in primary human esophageal cancers
SO Cancer Res., 48(18), 5119-23
AU Hollstein, M. C.; Smits, A. M.; Galiana, C.; Yamasaki, H.; Bos, J. L.; Mandard, A.; Partensky, C.; Montesano, R.
PY 1988

L12 ANSWER 15 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA109(11):87913r
TI Cytogenetic effects caused by phorbol ester tumor promoters in primary mouse keratinocyte cultures: correlation with the convertogenic activity of TPA in multistage skin carcinogenesis
SO Carcinogenesis (London), 9(7), 1207-15
AU Petrusevska, Rule T.; Fuerstenberger, Gerhard; Marks, Friedrich; Fusenig, Norbert E.
PY 1988

L12 ANSWER 16 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA109(9):68158g
TI A simple approach to prenatal diagnosis of .beta.-thalassemia in a geographic area where multiple mutations occur
SO Blood, 71(5), 1357-60
AU Cai, Shiping; Zhang, Jizeng; Huang, Daohua; Wang, Zhongxiang; Kan, Yuet Wai
PY 1988

L12 ANSWER 17 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA109(1):394a
TI Time course of sister chromatid exchanges and gene amplification induced by 1-.beta.-D-arabinofuranosylcytosine in V79-AP4 Chinese hamster cells
SO Chromosoma, 96(4), 306-10
AU Caligo, M. A.; Piras, A.; Rainaldi, G.
PY 1988

L12 ANSWER 18 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA108(9):72773a
TI Hamster cells with increased rates of DNA amplification, a new phenotype
SO Cell (Cambridge, Mass.), 48(5), 837-45
AU Giulotto, Elena; Knights, Catherine; Stark, George R.
PY 1987

L12 ANSWER 19 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA107(25):230476s
TI Cadaverine supplementation during a phor

difluoromethylornithine allows an overexpression, but prevents gene amplification, of ornithine decarboxylase in L1210 mouse leukemia cells
SO Biochem. J., 247(3), 651-5
AU Alhonen-Hongisto, Leena; Hirvonen, Ari; Sinervirta, Riitta; Jaenne, Juhani
PY 1987

L12 ANSWER 20 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA107(17):150369u
TI Induction of asynchronous replication of polyoma DNA in rat cells by ultraviolet irradiation and the effects of various inhibitors
SO Cancer Res., 47(17), 4565-70
AU Ronai, Zeev A.; Lambert, Michael E.; Johnson, Mark D.; Okin, Esther; Weinstein, I. Bernard
PY 1987

L12 ANSWER 21 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA107(15):128128t
TI Amplification of specific DNA sequences correlates with resistance of the archaebacterium Halobacterium volcanii to the dihydrofolate reductase inhibitors trimethoprim and methotrexate
SO MGG, Mol. Gen. Genet., 208(3), 518-22
AU Rosenshine, Ilan; Zusman, Tal; Werczberger, Ruth; Mevarech, Moshe
PY 1987

L12 ANSWER 22 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA106(7):44997s
TI Analysis of enzymically amplified .beta.-globin and HLA-DQ.alpha. DNA with allele-specific oligonucleotide probes
SO Nature (London), 324(6093), 163-6
AU Saiki, Randall K.; Bugawan, Teodorica L.; Horn, Glenn T.; Mullis, Kary B.; Erlich, Henry A.
PY 1986

L12 ANSWER 23 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA105(3):17640t
TI Methotrexate resistance and gene amplification. Mechanisms and implications
SO Cancer (Philadelphia), 57(10), 1912-17
AU Schimke, Robert T.
PY 1986

L12 ANSWER 24 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA104(5):32738d
TI Use of a P815-derived line with an amplified adenosine deaminase gene: an improved target for cellular cytotoxicity
SO Eur. J. Immunol., 15(10), 981-5
AU Vielh, Philippe; Castellazzi, Marc
PY 1985

L12 ANSWER 25 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA104(5):29781g

TI Enzymic amplification of beta-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia
SO Science (Washington, D. C., 1883-), 230(4732), 1350-4
AU Saiki, Randall K.; Scharf, Stephen; Faloona, Fred; Mullis, Kary B.; Horn, Glenn T.; Erlich, Henry A.; Arnheim, Norman
PY 1985

L12 ANSWER 26 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA104(1):374r
TI Selective overproduction of human dihydrofolate reductase in a methotrexate-resistant human-mouse somatic cell hybrid
SO Biochem. Biophys. Res. Commun., 132(2), 795-803
AU Sastry, K. J.; Chan, Tehsheng; Rodriguez, Lewis V.
PY 1985

L12 ANSWER 27 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA103(25):207859c
TI Analysis of dihydrofolate reductase gene amplification in a methotrexate-resistant human tumor cell line
SO Cancer Genet. Cytogenet., 17(4), 289-300
AU Meltzer, Paul S.; Cheng, Yung Chi; Trent, Jeffrey M.
PY 1985

L12 ANSWER 28 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA103(5):35372v
TI Characterization of single step albizziin-resistant Chinese hamster ovary cell lines with elevated levels of asparagine synthetase activity
SO J. Biol. Chem., 260(12), 7523-7
AU Andrulis, Irene L.; Evans-Blackler, Susan; Siminovitch, Louis
PY 1985

L12 ANSWER 29 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA103(5):32964d
TI Frequency of molecular alterations affecting ras protooncogenes in human urinary tract tumors
SO Proc. Natl. Acad. Sci. U. S. A., 82(11), 3849-53
AU Fujita, Jun; Srivastava, Shiv K.; Kraus, Matthias H.; Rhim, Johng S.; Tronick, Steven R.; Aaronson, Stuart A.
PY 1985

L12 ANSWER 30 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA102(21):178617u
TI Drug resistance to cancer chemotherapy
SO Med. Actual., 20(12), 657-63
AU Harris, A. L.
PY 1984

L12 ANSWER 31 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA102(1):3351a
TI Isolation of methotrexate-resistant cell lines in Petunia hybrida upon stepwise selection procedure
SO Plant Mol. Biol., 3(5), 303-11
AU Barg, Rivka; Peleg, Naomi; Perl, Meir; Beckmann, Jacques S.
PY 1984

L12 ANSWER 32 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA100(13):97549e
TI Moderate-level gene amplification in methotrexate-resistant Chinese hamster ovary cells is accompanied by chromosomal translocations at or near the site of the amplified DHFR gene
SO Mol. Cell. Biol., 4(1), 69-76
AU Flintoff, Wayne F.; Livingston, Elizabeth; Duff, Catherine; Worton, Ronald G.
PY 1984

L12 ANSWER 33 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA99(11):83667r
TI Amplification of the aroA gene from Escherichia coli results in tolerance to the herbicide glyphosate
SO Appl. Environ. Microbiol., 46(1), 37-43
AU Rogers, S. G.; Brand, L. A.; Holder, S. B.; Sharps, E. S.; Brackin, M. J.
PY 1983

L12 ANSWER 34 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA98(17):137290n
TI Unstable methotrexate resistance in human small-cell carcinoma associated with double minute chromosomes
SO N. Engl. J. Med., 308(4), 199-202
AU Curt, Gregory A.; Carney, Desmond N.; Cowan, Kenneth H.; Jolivet, Jacques; Bailey, Brenda D.; Drake, James C.; Kao-Shan, Chien Song; Minna, John D.; Chabner, Bruce A.
PY 1983

L12 ANSWER 35 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA97(25):207942g
TI Dihydrofolate reductase gene amplification and possible rearrangement in estrogen-responsive methotrexate-resistant human breast cancer cells
SO J. Biol. Chem., 257(24), 15079-86
AU Cowan, Kenneth H.; Goldsmith, Merrill E.; Levin, Richard M.; Aitken, Susan C.; Douglass, Edwin; Clendeninn, Neil; Nienhuis, Arthur W.; Lippman, Marc E.
PY 1982

L12 ANSWER 36 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA96(7):45968v
TI Toxicity of methotrexate and metoprine in a dihydrofolate reductase gene-amplified mouse cell line
SO Mol. Pharmacol., 20(3), 637-43
AU Hamrell, Michael; Laszlo, John; Brown, Oliver E.; Sedwick, W. David
PY 1981

L12 ANSWER 37 OF 39
COPYRIGHT (C) 1990 AMERICAN CHEMICAL SOCIETY

AN CA93(13):127191p
TI Aspects of cytoplasmic and environmental influences on gene expression
SO [illegible]

[illegible]
Prescott, David M. Academic: New York, N. Y.
AU Rae, Peter M. M.
PY 1980

L12 ANSWER 38 OF 39

AN CA93(9):92588u
TI Antifolate-resistant Chinese hamster cells. Evidence for dihydrofolate reductase gene amplification among independently derived sublines overproducing different dihydrofolate reductases
SO J. Biol. Chem., 255(14), 7024-8
AU Melera, Peter W.; Lewis, John A.; Biedler, June L.; Hession, Catherine
PY 1980

L12 ANSWER 39 OF 39

AN CA90(21):164558x
TI Moloney leukemia virus gene expression and gene amplification in preleukemic and leukemic BALB/Mo mice
SO Virology, 93(1), 80-90
AU Jaenisch, Rudolf
PY 1979

1. 4,319,216, Mar. 9, 1982, Discharge resistor; Toshio Ikeda, et al., 338*61; 310*72; 338*62, 282, 304 [IMAGE AVAILABLE]

US PAT NO: 4,319,216 [IMAGE AVAILABLE] L1: 1 of 1

ABSTRACT:
A discharge resistor adapted to be mounted on a rotatable shaft of a dynamo-electric device comprises a pair of spirally wound, insulated resistor

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US PAT NO: 4,319,216 [IMAGE AVAILABLE] L1: 1 of 1
elements and means for supporting these elements approximately coaxially with the shaft. Each of the resistor elements is spirally wound in a flatwise manner with a bore having an effective diameter greater than that of the shaft, and insulation layers are provided between adjacent turns thereof. The resistor elements are arranged and connected electrically in series such that the inductive impedance appearing across the respective resistor elements effectively cancel each other.

=>

=> s 4319216/pn
L2 1 4319216/PN

=> d l2 cit,ab

1. 4,319,216, Mar. 9, 1982, Discharge resistor; Toshio Ikeda, et al., 338*61; 310*72; 338*62, 282, 304 [IMAGE AVAILABLE]

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US PAT NO: 4,319,216 [IMAGE AVAILABLE] L2: 1 of 1

ABSTRACT:
A discharge resistor adapted to be mounted on a rotatable shaft of a dynamo-electric device comprises a pair of spirally wound, insulated resistor elements and means for supporting these elements approximately coaxially with the shaft. Each of the resistor elements is spirally wound in a flatwise manner with a bore having an effective diameter greater than that of the shaft, and insulation layers are provided between adjacent turns thereof. The resistor elements are arranged and connected electrically in series such that the inductive impedance appearing across the respective resistor elements effectively cancel each other.

=> s amplifiable(w)marker?
37 AMPLIFIABLE

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11882 MARKER?
L3 5 AMPLIFIABLE(W)MARKER?

=> d l3 1-5 cit

1. 4,912,040, Mar. 27, 1990, Eucaryotic expression system; Randal J. Kaufman, et al., 435*69.6, 69.1, 91, 172.1, 172.3, 240.1, 240.2, 240.4, 252.3, 320; 935*11, 32, 34, 61, 67, 68, 69, 70

2. 4,879,227, Nov. 7, 1989, Production of a recombinant human colony stimulating factor; Steven C. Clark, et al., * ; 435*172.3, 320; 536*27; 935*9, 11, 13

3. 4,877,864, Oct. 31, 1989, Osteoinductive factors; Elizabeth A. Wang, et al., 530*324; 435*69.1, 172.3, 320; 514*12; 935*13

4. 4,877,729, Oct. 31, 1989, Recombinant DNA encoding novel family of primate hematopoietic growth factors; Steven C. Clark, et al., 435*69.52,

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69.5, 172.3, 320; 935*9, 10, 11, 13

5. 4,868,119, Sep. 19, 1989, Hematopoietic growth factors; Steven C. Clark, et al., 435*240.2, 172.3, 252.31, 252.33, 320; 536*27; 935*9, 11, 13

=> d l3 1-5 cit,ab

1. 4,912,040, Mar. 27, 1990, Eucaryotic expression system; Randal J. Kaufman, et al., 435*69.6, 69.1, 91, 172.1, 172.3, 240.1, 240.2, 240.4, 252.3, 320; 935*11, 32, 34, 61, 67, 68, 69, 70

US PAT NO: 4,912,040 L3: 1 of 5

ABSTRACT:
This invention provides vectors, improved host cells and improved methods for producing a heterologous protein by culturing an improved eucaryotic host cell of this invention transformed or transfected with a vector capable of

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US PAT NO: 4,912,040 L3: 1 of 5
directing the expression of the heterologous protein. The preferred improved host cell of this invention is a mammalian host cell containing and capable of expressing an anti-sense GRP78 DNA sequence.

2. 4,879,227, Nov. 7, 1989, Production of a recombinant human colony stimulating factor; Steven C. Clark, et al., * ; 435*172.3, 320; 536*27; 935*9, 11, 13

US PAT NO: 4,879,227 L3: 2 of 5

ABSTRACT:
A process for producing a novel protein, CSF-69, is provided. The protein is capable of stimulating proliferation of monocytic lineage types cells in vitro assays. A novel DNA sequence codes on expression for CSF-69.

3. 4,877,864, Oct. 31, 1989, Osteoinductive factors; Elizabeth A. Wang, et

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al., 530*324; 435*69.1, 172.3, 320; 514*12; 935*13

US PAT NO: 4,877,864 L3: 3 of 5

ABSTRACT:
Human and bovine bone inductive factors are provided. Such factors may be produced by recombinant techniques and be useful in the treatment of bone defects.

4. 4,877,725, Oct. 31, 1989, Recombinant DNA

primate hematopoietic growth factors; Steven C. Clark, et al., 435*69.52, 69.5, 172.3, 320; 935*9, 10, 11, 13

US PAT NO: 4,877,729 L3: 4 of 5

ABSTRACT:
A novel family of primate IL-3-like polypeptides is provided via recombinant

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US PAT NO: 4,877,729 L3: 4 of 5
techniques.

5. 4,868,119, Sep. 19, 1989, Hematopoietic growth factors; Steven C. Clark, et al., 435*240.2, 172.3, 252.31, 252.33, 320; 536*27; 935*9, 11, 13

US PAT NO: 4,868,119 L3: 5 of 5

ABSTRACT:
A novel family of primate CSF-1-like polypeptides is provided via recombinant techniques.

=> s pntd
L4 0 PNTD

=> s puc19

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L5 43 PUC19

=> s skoultchi, arthur i?inv
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'I?INV'

=> s skoultchi,arthur i/inv
L6 0 SKOULTCHI,ARTHUR I/INV

=> s clonal(w)expansion?
267 CLONAL
88790 EXPANSION?
L7 17 CLONAL(W)EXPANSION?

=> s 17 and homologous(w)recombination
2812 HOMOLOGOUS
4834 RECOMBINATION

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52 HOMOLOGOUS(W)RECOMBINATION
L8 0 L7 AND HOMOLOGOUS(W)RECOMBINATION

=> s homologous(w)recombination
2812 HOMOLOGOUS
4834 RECOMBINATION
L9 52 HOMOLOGOUS(W)RECOMBINATION

=> s 19 and protein(w)expression
22039 PROTEIN

103 PROTEIN(W)EXPRESSION
L10 3 L9 AND PROTEIN(W)EXPRESSION

=> d l10 1-3 cit,ab

1. 4,784,941, Nov. 15, 1988, Expression and diagnostic use of pENV-3 encoded peptides which are immunologically reactive with antibodies to LAV; Susan M.

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Watanabe, et al., 435*5, 7, 69.3; 436*531, 811; 530*324, 325, 326, 327, 328, 329

US PAT NO: 4,784,941 L10: 1 of 3

ABSTRACT:
A method of expressing peptides which are immunologically reactive with antibodies to LAV is disclosed. The peptides are produced by bacterial host cells transformed with a recombinant plasmid which includes appropriate procaryotic transcriptional and translational signals for expression, followed by a DNA sequence coding for a peptide comprising the amino acid sequence as shown in FIG. 5 starting with isoleucine, number 1, and ending with threonine, number 173. The peptides of the present invention are immunologically reactive with antibodies to LAV, or antibodies to viruses defined to be the same as or equivalent to LAV. The peptides produced by the method disclosed may be used to screen for the presence of antibodies to LAV in a biological fluid, to determine the presence of LAV antigen in a

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US PAT NO: 4,784,941 L10: 1 of 3
biological fluid, or within a method for producing antibodies to LAV through the immunization of an animal with the peptide. Further, the pNEV-3 encoded peptides may be used as a vaccine against infection by the causative virus for acquired immune deficiency syndrome.

2. 4,771,002, Sep. 13, 1988, Transcription in plants and bacteria; Stanton B. Gelvin, 435*172.3, 252.2, 252.33, 320; 935*30, 35, 56, 72

US PAT NO: 4,771,002 L10: 2 of 3

ABSTRACT:
A promoter region that drives expression of a 1450 base T.sub.R transcript in octopine-type crown gall tumors can also promote expression of a foreign structural gene in bacteria. Use of this dul-purpose promoter region to drive expression of a single copy of a foreign structural gene in both plants and bacteria is taught. The construction of a selectable marker functional in

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US PAT NO: 4,771,002 L10: 2 of 3
eukaryotes and prokaryotes is exemplified, as are vectors useful in efforts to transform plants.

3. 4,405,712, Sep. 20, 1983, LTR-Vectors; George F. Vande Woude, et al., 435*5, 69.1, 69.3, 172.3, 235, 240.2, 320; 935*9, 19, 23, 32, 57

US PAT NO: 4,405,712 L10: 3 of 3

ABSTRACT:
The production of vectors composed of portions of retrovirus, particularly of

[illegible] genes and additional viral sequences which can "rescue" these genes into a replicating virus particle.

=>

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transfectants. These secondary transfectants will lose large amounts of the nonessential DNA found in **primary** **transfectants**, thus identifying the DNA containing essential oncogenic regions.

```
=> s secondary(w)transfectant?
        145154 SECONDARY
            36 TRANSFECTANT?
L2           2 SECONDARY(W)TRANSFECTANT?

=> d l2 1-2 cit

1.  4,935,341, Jun. 19, 1990, Detection of point mutations in neu genes;
Cornelia I. Bargmann, et al., 435/6, 803; 436/501; 536/27; 935/9, 78
[IMAGE AVAILABLE-

2.  4,652,522, Mar. 24, 1987, Continuous lymphocyte cell lines, their
production and use; Roger H. Kennett, et al., 435/69.6, 172.1, 240.27,
948; 935/52

=> d l2 2 kwic

US PAT NO:     4,652,522                              L2: 2 of 2

SUMMARY:

BSUM(26)

 It . . . DNA portions containing the operative oncogene(s) can be
identified by transfecting additional lymphocytes with DNA from the
primary transfectants. These **secondary** **transfectants** will lose
large amounts of the nonessential DNA found in primary transfectants,
thus identifying the DNA containing essential oncogenic regions.

=> s selectable(w)marker?
         20941 SELECTABLE
         15400 MARKER?
L3         248 SELECTABLE(W)MARKER?

=> s l3 and l1 or l2
L4           2 L3 AND L1 OR L2

=> d l4 1-2 cit

1.  4,935,341, Jun. 19, 1990, Detection of point mutations in neu genes;
Cornelia I. Bargmann, et al., 435/6, 803; 436/501; 536/27; 935/9, 78
[IMAGE AVAILABLE-

2.  4,652,522, Mar. 24, 1987, Continuous lymphocyte cell lines, their
production and use; Roger H. Kennett, et al., 435/69.6, 172.1, 240.27,
948; 935/52

=> d l4 1-2 kwic

US PAT NO:     4,935,341 [IMAGE AVAILABLE-            L4: 1 of 2

DETDESC:
```

DETD(22)

This . . . et al., Nature, 277: 108-114 (1979). A transforming neu cDNA clone derived from the B104-1-1 cell line, which is a **secondary** **transfectant** of an activated rat neu gene, was inserted into pSV2 to create a plasmid designated as pSV2neuT (FIG. 1). pSV2neuT. . .

US PAT NO: 4,652,522 L4: 2 of 2

SUMMARY:

BSUM(26)

It . . . DNA portions containing the operative oncogene(s) can be identified by transfecting additional lymphocytes with DNA from the primary transfectants. These **secondary** **transfectants** will lose large amounts of the nonessential DNA found in primary transfectants, thus identifying the DNA containing essential oncogenic regions.

=> s hygromycin(w)b?
TRUNCATION LIMITS EXCEEDED - SEARCH ENDED

=> s hygromycin?
L5 96 HYGROMYCIN?

=> s l5 and selectable(w)marker?
20941 SELECTABLE
15400 MARKER?
248 SELECTABLE(W)MARKER?
L6 38 L5 AND SELECTABLE(W)MARKER?

=> s l6 and l1imary
L7 0 L6 AND L1

=> s l6 and primary(w)transfectant?
268473 PRIMARY
36 TRANSFECTANT?
2 PRIMARY(W)TRANSFECTANT?
L8 0 L6 AND PRIMARY(W)TRANSFECTANT?

=> s l6 and l2
L9 0 L6 AND L2

=> s l5 and DHFR?
117 DHFR?
L10 8 L5 AND DHFR?

=> d l10 1-8 cit

1. 4,975,369, Dec. 4, 1990, Recombinant and chimeric KS1/4 antibodies directed against a human adenocarcinoma antigen; Lisa S. Beavers, et al., 435/69.1, 172.3, 240.1; 530/387; 536/27; 935/41, 70, 71 [IMAGE AVAILABLE-

2. 4,966,849, Oct. 30, 1990, CDNA and genes for human angiogenin (angiogenesis factor) and methods of expression; Bert L. Vallee, et al.,

435/199, 172.3, 240.25, 252.3; 530/399; 536/27; 935/13, 14, 28, 29, 70, 71, 73 [IMAGE AVAILABLE-

3. 4,960,700, Oct. 2, 1990, Compositions and methods for the synthesis and assay of a mammalian enkephalinase; Bernard Malfroy-Camine, et al., 435/172.3, 212, 219, 240.2, 252.33 [IMAGE AVAILABLE-

4. 4,959,318, Sep. 25, 1990, Expression of protein C; Donald C. Foster, et al., 435/172.3, 226, 240.25, 320.1, 849; 536/27; 935/14, 29, 32, 48 [IMAGE AVAILABLE-

5. 4,956,288, Sep. 11, 1990, Method for producing cells containing stably integrated foreign DNA at a high copy number, the cells produced by this method, and the use of these cells to produce the polypeptides coded for by the foreign DNA; James G. Barsoum, 435/172.3, 69.1, 70.1, 71.1, 172.1, 252.3; 935/16, 33, 52 [IMAGE AVAILABLE-

6. 4,916,073, Apr. 10, 1990, CDNA and gene for human angiogenin (angiogenesis factor) and methods of expression; Bert L. Vallee, et al., 435/252.3, 172.3, 252.33, 320.1; 935/13, 72, 73

7. 4,784,949, Nov. 15, 1988, Universal dominant selectable marker cassette; David H. Gelfand, et al., 435/34, 69.3, 69.7, 172.3, 252.31, 252.33, 252.34, 254, 255, 320.1; 536/27; 930/10, 240, 310; 935/14, 27, 28, 29, 47

8. 4,721,672, Jan. 26, 1988, CDNA and gene for human angiogenin (angiogenesis factor) and methods of expression; Bert L. Vallee, et al., 435/69.1, 172.3, 255, 320.1; 514/12; 536/27; 930/10; 935/11, 13 [IMAGE AVAILABLE-

=> d l10 1-8 kwic

US PAT NO: 4,975,369 [IMAGE AVAILABLE- L10: 1 of 8

SUMMARY:

BSUM(18)

dhfr--the dihydrofolate reductase phenotype or gene conferring same.

SUMMARY:

BSUM(26)

Hm.sup.R --the **hygromycin**-resistant phenotype or gene conferring same.

DETDESC:

DETD(54)

The BK enhancer-type vector of the present invention comprises a BK enhancer-adenovirus late promoter cassette plus a **hygromycin** resistance conferring gene and a murine dihydrofolate reductase (**dhfr**) gene. The use of the BK virus enhancer in conjunction with the

adenovirus late promoter significantly increases transcription of a recombinant gene in eukaryotic host cells. The **hygromycin** resistance-conferring gene is present as a selectable marker for use in eukaryotic host cells. The murine dihydrofolate reductase gene, under. . . This amplification, described in a review by Schimke, 1984, Cell 37:705-713, can also involve DNA sequences closely contiguous with the **dhfr** gene. The **dhfr** gene is a selectable marker in **dhfr**-negative cells and can be used to increase the copy number of a DNA segment by exposing the host cell to. . .

DETDESC:

DETD(55)

Plasmid . . . to construct a eukaryotic expression vector for expression of the novel KS1/4 of the present invention. Plasmid pLPChd contains the **dhfr** gene, the Adenovirus type-2 promoter and the BK virus enhancer. The BK virus, which contains the BK virus enhancer, can. . .

DETDESC:

DETD(61)

Episomal . . . host cells. This was done by ligating plasmid pLPC to a portion of plasmid pSV2hyg, a plasmid that comprises a **hygromycin** resistance-conferring gene. Plasmid pSV2hyg can be obtained from the Northern Regional Research Laboratory (NRRL), Peoria, IL 61640, under the accession. . .

DETDESC:

DETD(62)

Plasmid pSV2hyg was digested with restriction enzyme BamHI, and the .about.2.5 kb BamHI restriction fragment, which comprises the entire **hygromycin** resistance-conferring gene, was isolated, treated with Klenow enzyme (the large fragment produced upon subtilisin cleavage of E. coli DNA polymerase. . . pLPC to yield plasmids pLPChyg1 and pLPChyg2. Plasmids pLPChyg1 and pLPChyg2 differ only with respect to the orientation of the **hygromycin** resistance-conferring fragment. Plasmid pLPChyg1 contains an .about.5.0 kb HindIII fragment whereas plasmid pLPChyg2 contains an .about.1.0 kb fragment. The construction. . .

DETDESC:

DETD(63)

Plasmid pBW32, which contains the murine dihydrofolate reductase (**dhfr**) gene, was constructed next. Plasmid pTPA102 (NRRL B-15834) was cut with restriction enzyme TthIIII and the .about.4.4 kb restriction fragment. . .

DETDESC:

DETD(66)

Plasmid . . . by ligating the .about.2.0 kb HindIII-BglII fragment of plasmid pTPA103 to the .about.4.2 kb HindIII-BglII fragment of plasmid pSV2-.beta.-globin. Plasmid pSV2-**dhfr** (ATCC 37146) was cut with restriction enzyme PvuII. Following the addition of BamHI linkers, the .about.1.9 kb **dhfr** gene-containing fragment was ligated into BamHI cut, phosphatased plasmid pTPA301 to form plasmid pTPA303. Plasmid pTPA301 was cut with restriction. . . yield an .about.2.7 kb fragment. Plasmid pTPA303 was cut with restriction enzymes HindIII and EcoRI to yield the .about.2340 bp **dhfr** gene containing fragment. Plasmid pTPA303 was cut with restriction enzymes HindIII and SstI to yield an .about.1.7 kb fragment. Plasmid. . .

DETDESC:

DETD(67)

The **dhfr** gene-containing, .about.1.9 kb BamHI restriction fragment of plasmid pBW32 was isolated, treated with Klenow enzyme, and inserted into partially-EcoRI-digested plasmid pLPChyg1 to yield plasmids pLPChd1 and pLPChd2. Plasmid pLPChyg1 contains two EcoRI restriction enzyme recognition sites, one in the **hygromycin** resistance-conferring gene and one in the plasmid pBR322-derived sequences. The fragment comprising the **dhfr** gene was inserted into the EcoRI site located in the pBR322-derived sequences of plasmid pLPChyg1 to yield plasmids pLPChd1 and. . . the accompanying drawings. The construction of plasmids pLPChd1 and pLPChd2, which differ only with respect to the orientation of the **dhfr** gene-containing DNA segment, is described in Example 17.

DETDESC:

DETD(203)

About . . . and then was extracted twice with chloroform. The BamHI-digested plasmid pSV2hyg DNA was loaded onto an agarose gel, and the **hygromycin** resistance gene-containing, .about.2.5 kb restriction fragment was isolated in substantial accordance with the procedure described in Example 12A.

DETDESC:

DETD(261)

Plasmid pSV2-**dhfr** comprises a dihydrofalate reductase (**dhfr**) gene useful for selection of transformed eukaryotic cells and amplification of DNA covalently linked to the **dhfr** gene. Ten .mu.g of plasmid pSV2-**dhfr** (isolated from E. coli K12 HB101/pSV2-**dhfr**, ATCC 37146) were mixed with 10 .mu.l 10X PvuII buffer, 2 .mu.l (.about.20 units) PvuII restriction enzyme, and 88 .mu.l. . . at 37.degree. C. for two hours. The reaction was terminated by phenol and chloroform extractions, and then, the PvuII-digested plasmid pSV2-**dhfr** DNA was precipitated and collected by centrifugation.

DETDESC:

DETD(262)

BamHI . . . then incubated at 37.degree. for 60 minutes and stored at -20.degree. C. Five .mu.l (.about.5 .mu.g) of the PvuII-digested plasmid pSV2-**dhfr** and 12 .mu.l (.about.0.25 .mu.g) of the kinased BamHI linkers were mixed and incubated with 11 .mu.l of H.sub.2 O,. . .

DETDESC:

DETD(263)

Ten . . . 3 hours. The reaction was loaded onto a 1% agarose gel, and the desired .about.1.9 kb fragment, which comprises the **dhfr** gene, was isolated from the gel. All linker additions performed in these examples were routinely purified on an agarose gel. . .

DETDESC:

DETD(264)

Next, . . . 20 .mu.l H.sub.2 O. Ten .mu.l (.about.0.25 .mu.g) of phosphatased plasmid pTPA301 were added to 5 .mu.l of the BamHI, **dhfr**-gene-containing restriction fragment (.about.1.5 .mu.g), 3 .mu.l of 10X ligase buffer, 3 .mu.l (.about.1500 units) of T4 DNA ligase, and 9. . .

DETDESC:

DETD(267)

To isolate a restriction fragment that comprises the **dhfr** gene, plasmid pTPA303 was double-digested with HindIII and EcoRI restriction enzymes, and the .about.2340 bp EcoRI-HindIII restriction fragment that comprises the **dhfr** gene was isolated and recovered.

DETDESC:

DETD(273)

About . . . until the digestion products were clearly separated. The .about.1.9 kb Klenow-treated, BamHI restriction fragment of plasmid pBW32 that comprises the **dhfr** gene was isolated from the gel and prepared for ligation in substantial accordance with the procedure of Example 12A. About. . .

DETDESC:

DETD(274)

About . . . partial EcoRI digestion. Plasmid pLPChygl has two EcoRI restriction sites, one of which is within the coding sequence of the **hygromycin** resistance-conferring (HmR) gene, and it was desired to insert the **dhfr**-gene.-containing restriction fragment into the EcoRI site of plasmid pLPChygl that is not in the HmR gene. The partially-EcoRI-digested plasmid pLPChygl. . .

DETDESC:

DETD(275)

About . . . plasmids pLPChd1 and pLPChd2, which differ only with respect to the orientation of the .about.1.9 kb fragment that comprises the **dhfr** gene.

DETDESC:

DETD(325)

For cells transfected with plasmids containing the **hygromycin** resistance-conferring gene, **hygromycin** is added to the growth medium to a final concentration of about 200 to 400 .mu.g/ml. The cells are then incubated at 37.degree. C. for 2-4 weeks with medium changes at 3 to 4 day intervals. The resulting **hygromycin**-resistant colonies are transferred to individual culture flasks for characterization. The selection of neomycin (G418 is also used in place of neomycin)-resistant colonies is performed in substantial accordance with the selection procedure for **hygromycin**-resistant cells, except that neomycin is added to a final concentration of 400 .mu.g/ml rather than **hygromycin**. 293 cells are **dhfr** positive, so 293 transformants that contain plasmids comprising the **dhfr** gene are not selected solely on the basis of the **dhfr**-positive phenotype, which is the ability to grow in media that lacks hypoxanthine and thymine. Cell lines that do lack a functional **dhfr** gene and are transformed with **dhfr**-containing plasmids can be selected for on the basis of the **dhfr***+ phenotype.

DETDESC:

DETD(326)

The use of the dihydrofolate reductase (**dhfr**) gene as a selectable marker for introducing a gene or plasmid into a **dhfr**-deficient cell line and the subsequent use of methotrexate to amplify the copy number of the plasmid has been well established in the literature. Although the use of **dhfr** as a selectable and amplifiable marker in **dhfr**-producing cells has not been well studied, evidence in the literature would suggest that **dhfr** can be used as a selectable marker in **dhfr**-producing cells and for gene amplification. The use of the present invention is not limited by the selectable marker used. Moreover,. . . utilized. In 293 cells, it is advantageous to transform with a vector that contains a selectable marker such as the **hygromycin** B resistance-conferring gene and then amplify using methotrexate, which cannot be used for selection of murine **dhfr**-containing plasmids in 293 cells.

DETDESC:

DETD(327)

Cell . . . unlike 293 cells, AV12 cells were directly selected with methotrexate (200-500 nM) when transformed with a vector containing the murine **dhfr** gene. To express a heavy chain, it was necessary to transform the AV12 cells with any expression vector which encodes. . .

US PAT NO: 4,966,849 [IMAGE AVAILABLE- L10: 2 of 8

DRAWING DESC:

DRWD(5)

FIG. 4 illustrates the construction of the mammalian cell expression vector pHAGF-MT-**DHFR**.

DETDESC:

DETD(26)

Cloned . . . cells along with the gene of interest. Preferred selectable markers include genes that confer resistance to drugs, such an neomycin, **hygromycin**, and methotrexate. Selectable markers may be introduced into the cell on a separate plasmid at the same time as the. . .

DETDESC:

DETD(46)

For expressing angiogenin in transfected mammalian cells, expression vector pHAGF-MT-**DHFR**, comprising the angiogenin genomic coding sequence (HAGF), the mouse metallothionein.1 (MT.1) promoter, and a **DHFR** selectable marker joined to the SV40 promoter, was constructed.

DETDESC:

DETD(48)

The . . . and Hemostasis 54:282, 1985), comprising the mouse metallothionein (MT-1) promoter, human Factor IX coding sequence, SV40 promoter, and a modified **DHFR** gene (Levinson et al., EPO publication 117,060) was digested with BamHI and EcoRI (FIG. 4). The fragment comprising the pUC13 sequence and the SV40-**DHFR** expression unit was gel purified. This fragment was then joined to the BamHI-EcoRI HAGF fragment. The resultant vector was designated pHAGF-MT-**DHFR** (FIG. 4).

DETDESC:

DETD(49)

Plasmid pHAGF-MT-**DHFR** was then transferred into baby hamster kidney (BHK) cells by standard calcium phosphate-mediated transfection procedures. Cells containing the vector were. . .

US PAT NO: 4,960,700 [IMAGE AVAILABLE- L10: 3 of 8

DETDESC:

DETD(32)

Expression . . . contain a selection gene, also termed a selectable marker. Examples of suitable selectable markers for mammalian cells are

dihydrofolate reductase (**DHFR**), thymidine kinase or neomycin. When such selectable markers are successfully transferred into a mammalian host cell, the transformed mammalian host. . . of a mutant cell line which lacks the ability to grow independent of a supplemented media. Two examples are: CHO **DHFR**.sup.- cells and mouse LTK.sup.- cells. These cells lack the ability to grow without the addition of such nutrients as thymidine. . . the missing nucleotides are provided in a supplemented media. An alternative to supplementing the media is to introduce an intact **DHFR** or TK gene into cells lacking the respective genes, thus altering their growth requirements. Individual cells which were not transformed with the **DHFR** or TK gene will not be capable of survival in non supplemented media.

DETDESC:

DETD(33)

The . . . J. Molec. Appl. Genet. 1: 327 (1982), mycophenolic acid, Mulligan, R. C. and Berg, P. Science 209: 1422 (1980) or **hygromycin**, Sugden, B. et al., Mol. Cell. Biol. 5: 410-413 (1985). The three examples given above employ bacterial genes under eukaryotic control to convey resistance to the appropriate drug G418 or neomycin (geneticin), xgpt (mycophenolic acid) or **hygromycin**, respectively.

DETDESC:

DETD(34)

"Amplification" . . . an isolated region within a cell's chromosomal DNA. Amplification is achieved using a selection agent e.g. methotrexate (MTX) which inactivates **DHFR**. Amplification or the making of successive copies of the **DHFR** gene results in greater amounts of **DHFR** being produced in the face of greater amounts of MTX. Amplification pressure is applied notwithstanding the presence of endogenous **DHFR**, by adding ever greater amounts of MTX to the media. Amplification of a desired gene can be achieved by cotransfecting a mammalian host cell with a plasmid having a DNA encoding a desired protein and the **DHFR** or amplification gene permitting cointegration. One ensures that the cell requires more **DHFR**, which requirement is met by replication of the selection gene, by selecting only for cells that can grow in the. . .

DETDESC:

DETD(35)

Preferred . . . F. L. et al. J. Gen. Virol. 36: 59 [1977[); baby hamster kidney cells (BHK, ATCC CCL 10); chinese hamster ovary-cells-**DHFR** (CHO, Urlaub and Chasin, PNAS (U.S.A.) 77: 4216, [1980-); mouse sertoli cells (TM4, Mather, J. P., Biol. Reprod. 23: 243-251. . .

DETDESC:

DETD(140)

(2) . . . bp fragment isolated. This 5340 bp fragment contains the CMV enhancer, promoter, splice site, Amp.sup.R gene, E. coli origin, SV40 **DHFR** and the SV40 poly A site.

DETDESC:

DETD(146)

Human . . . with either of pCIS-Enksol or pCIS-Enkinsol, stable transformants selected and, if desired, amplified in conventional fashion by use of the **DHFR** marker donated from pCIStPA. Cytoplasmic domain-deleted enkephalinase is recovered from the transformant culture of pCIS-Enkinsol transformants. Cytoplasmic and transmembrane domain-deleted. . .

US PAT NO: 4,959,318 [IMAGE AVAILABLE- L10: 4 of 8

DRAWING DESC:

DRWD(12)

FIG. 11 illustrates the expression vector pD5(PC-**DHFR**.sup.r). **DHFR**.sup.r denotes the methotrexate resistant mutant dihydrofolate reductase gene sequence; pA denotes the SV40 late polyadenylation signal. Other symbols used are. . .

DETDESC:

DETD(31)

Cloned . . . cells along with the gene of interest. Preferred selectable markers include genes that confer resistance to drugs, such as neomycin, **hygromycin**, and methotrexate. Selectable markers may be introduced into the cell on a separate plasmid at the same time as the. . .

DETDESC:

DETD(60)

Plasmid . . . from plasmid pDHFRIII (Berkner and Sharp, Nuc. Acids. Res. 13: 841-857, 1985). The Pst I site immediately upstream from the **DHFR** sequence in pDHFRIII was converted to a Bcl I site by digesting 10 ug of plasmid with 5 units of. . .

DETDESC:

DETD(67)

A . . . protein C sequence from a polycistronic message is constructed by using pD5, a plasmid similar to pD3 which contains a **DHFR** coding sequence lacking most of the 5' non-coding region. The **DHFR** sequence is further modified to reduce its binding affinity to methotrexate.

DETDESC:

DETD(69)

The **DHFR** sequence is modified by first digesting pDHFRIII with Pst I and Sst I and isolating the 400 bp **DHFR** fragment. This is subcloned in an Mi3 phage vector and mutagenized as described by Simonsen and Levinson (Proc. Natl. Acad. Sci. USA 80: 2495-2499, 1983). Mutagenesis results in a single base pair change in the **DHFR** sequence. The altered fragment is then reinserted into pDHFRIII to produce plasmid pDHFR.sup.r III.

DETDESC:

DETD(70)

The 5' non-coding region of the **DHFR** sequence is then removed. Plasmid pDHFR.sup.r III is cleaved with Fnu 4HI, which cuts the plasmid at approximately 20 sites,. . . ends, and the mixture digested with Bam HI and Nco I. A 0.6 kb Bam HI-Nco I fragment comprising the **DHFR**.sup.r cDNA is isolated. Plasmid pDHFRIII is digested with Nco I and Bam HI and the 0.2 kb fragment comprising the SV40 polyadenylation signal is isolated. The polyadenylation signal, in the early orientation, is then ligated to the **DHFRr** fragment. After digestion with Bam HI, the resultant Bam HI fragment is then inserted into the Bam HI site of. . . used to transform E. coli HB101. plasmid DNA is prepared and screened by restriction endonuclease digestion. A plasmid having the **DHFR**.sup.r insert in the correct orientation for transcription from the Ad2 major late promoter is designated pD5 (**DHFR**.sup.r).

DETDESC:

DETD(71)

To express protein C using plasmid pD5(**DHFRr**), pMMC is digested with Eco RI and the i.5 kb protein C fragment is isolated. The Eco RI termini are converted to Bcl I termini by linkering. Plasmid pD5(**DHFR**.sup.r) is partially digested with Bam HI to cleave it at the 5' end of the **DHFR**.sup.r sequence and is ligated to the protein C fragment. Plasmid DNA is screened for the proper orientation and insertion of the protein C fragment. The resultant vector, designated pD5(PC-**DHFR**.sup.r), is illustrated in FIG. 11.

US PAT NO: 4,956,288 [IMAGE AVAILABLE- L10: 5 of 8

SUMMARY:

BSUM(7)

None . . . produce high copy number integrants. The most widely used procedure to obtain high copy number integrants utilizes the dihydrofolate reductase ("**DHFR**") gene.

SUMMARY:

BSUM(8)

Mammalian cells which contain multiple copies of the **DHFR** gene are selected when a culture of these cells is subjected to sequentially increasing concentrations of methotrexate (Alt et al.,. . . "Selective Multiplication of Dihydrofolate Reductase Genes in Methotrexate-Resistant Variants of Cultured Murine Cells", J. Biol. Chem., 253, pp. 1357-79 (1978)). **DHFR** is an essential enzyme for cell survival. Since methotrexate ("MTX") is a competitive inhibitor of DHRF, only those cells that have increased their **DHFR** content (e.g. by amplifying the resident DHRF gene) to offset MTX inhibition will survive. Furthermore, as the MTX concentration is sequentially increased, cells will require increasing amounts of **DHFR**, and thus higher **DHFR** gene copy numbers, to survive. This is the basis of the **DHFR** gene amplification procedure.

SUMMARY:

BSUM(9)

One indication that the **DHFR** gene might be useful in the amplification of the cotransfected genes was the report that when Escherichia coli plasmid pBR322 was cotransfected (introduced together) with genomic DNA containing a MTX-resistant **DHFR** gene into mouse cells, the pBR322 DNA was also amplified by MTX selection (Wigler et al., "Transformation of Mammalian Cells. . .

SUMMARY:

BSUM(10)

The generation of very high copy number integrants was made possible by the isolation of Chinese hamster cells deficient in native **DHFR** activity ("**DHFR**.sup.- CHO cells") (Urlaub and Chasin, "Isolation of Chinese Hamster Cell Mutants Deficient in Dihydrofolate Reductase Activity", Proc. Natl. Acad. Sci. USA, 77(7), 4216-20 (1980). Transfection of these **DHFR**.sup.- CHO cells with a plasmid containing both the **DHFR** gene and the E. coli gpt gene, followed by MTX selection, produced recombinant host cells which had amplified the gpt. . .

SUMMARY:

BSUM(11)

In a more dramatic example of the possibility for amplification of non-selectable genes using this technique, transfection of **DHFR**.sup.- CHO cells with plasmids containing both the murine **DHFR** gene and the SV40 early region, followed by sequential step-wise increases in the MTX concentration of the growth medium, produced. . .

SUMMARY:

BSUM(12)

While the **DHFR**/MTX amplification procedure produces cells with amplified copies of transfected DNA, it has several serious drawbacks. These drawbacks include the slowness of the procedure, the necessity of

using **DHFR**.sup.- cells to obtain significant amplification, and the fluidity of amplified DNA.

SUMMARY:

BSUM(14)

Another drawback of the **DHFR**/MTX amplification procedure is that it does not work well for cells that contain a **DHFR** gene ("**DHFR**.sup.+ cells"). At best, only a fifty-fold amplification of transfected DNA has been reported in **DHFR**.sup.+ cells (Wigler et al., "Transformation of Mammalian Cells with an Amplifiable Dominant-Acting Gene", Proc. Natl. Acad. Sci. USA, 77(6), pp. 3567-70 (1980)). The production of **DHFR**.sup.- cells from **DHFR**.sup.+ cells, if possible at all for a given cell type, is lengthy and laborious (Urlaub and Chasin, "Isolation of Chinese. . . Deficient in Dihydrofolate Reductase Activity", Proc. Natl. Acad. Sci. USA, 77(7), pp. 4216-20 (1980)). Since all mammalian cells possess the **DHFR** gene, a worker looking for significant amplification of transfected DNA would be restricted to using **DHFR**.sup.- CHO cells unless he was willing to face the ordeal of creating a new **DHFR**.sup.- cell type.

SUMMARY:

BSUM(15)

An additional drawback of **DHFR**/MTX amplification is that not all sequences contained within transfected DNA will be amplified to the same degree (Kaufman and Sharp,. . .

DRAWING DESC:

DRWD(2)

FIG. 1 is a pictorial representation of vector pSV2-**DHFR**

DETDESC:

DETD(14)

In . . . selective genes include: neo (G418 resistance), gpt (xanthine utilization in the presence of mycophenolic acid), hisD (histidinol utilization, and hygro (**hygromycin** B resistance).

DETDESC:

DETD(65)

DHFR.sup.- Gene Copy Number in CHO Cells

DETDESC:

DETD(67)

DHFR.sup.- CHO cells were subcloned from the clone designated CHO-DUKX-B1 of Urlaub and Chasin, "Isolation of Chinese Hamster Cell

Mutants Deficient. . .

DETDESC:

DETD(68)

For primary selection, **DHFR**.sup.- CHO cells were transferred to MEM alpha supplemented with 10% dialyzed fetal bovine serum (Hazleton) and 4 mM glutamine and. . .

DETDESC:

DETD(71)

The vector pSV2-**DHFR** (FIG. 1) expresses **DHFR** from the SV40 early promoter. The construction of this vector is described in Subramani et al., "Expression of the Mouse Dihydrofolate Reductase Complementary Deoxyribonucleic acid in Simian Virus 40 Vectors", Mol. Cell. Biol., 1(9), pp. 854-64 (1981). Vector pSV2-**DHFR**, harbored in E. coli strain HB101, is available from the American Type Culture Collection, Rockville, Md. (ATCC 37146).

DETDESC:

DETD(74)

Foreign DNA was prepared for transfer into host cells as follows. Two hundred micrograms of the vector pSV2-**DHFR** were digested overnight at 37.degree. C. with EcoRI to linearize the DNA (400 .mu.l reaction containing 200 .mu.g DNA and. . .

DETDESC:

DETD(75)

Each electroporation procedure utilized approximately 2.times.10.sup.7 **DHFR**.sup.- CHO cells. These cells were fed or passaged on the day prior to electroporation and were approximately 50% confluent on. . .

DETDESC:

DETD(77)

Cells . . . in .alpha..sup.- medium. The cells were incubated for four days in this primary selection medium (.alpha..sup.- medium). Approximately 15-30% of **DHFR**.sup.- CHO cells were stably transformed to .alpha..sup.- resistance under these conditions, indicating that these cells had incorporated at least one copy of foreign DNA and were expressing the **DHFR** gene. After the four-day primary selection, the plates became nearly confluent with growing .alpha..sup.- resistant cells (.alpha..sup.- sensitive cells detach. . .

DETDESC:

DETD(82)

Determination of **DHFR** Gene Copy Number

DETDESC:

DETD(85)

For . . . Harbor, N.Y. (1980)). Each gel also contained several lanes of plasmid standards. The standards consisted of digested (PvuII and BglII pSV2-**DHFR** corresponding to various **DHFR** copy numbers of between 1 and 1000 copies per cell (usually corresponding to 2, 10, 50, 250, and 1000 copies).. . . lane), we computed the amount of digested plasmid required to give a single copy hybridization signal as being 16 pg pSV2-**DHFR**. This number was confirmed by comparison with hybridization signals of genomic DNA from clones known to contain only a single copy of pSV2-**DHFR**.

DETDESC:

DETD(87)

The hybridization probe used was the .sup.32 P-labelled 1000 bp PvuII/BglII fragment of pSV2-**DHFR**. The gel-purified fragment was labelled with .sup.32 P according to the method of Feinberg and Vogelstein, "A Technique for Radiolabelling. . .

DETDESC:

DETD(90)

TABLE II

Effect of MTX Concentration on **DHFR** Gene Copy Number

[MTX- .mu.M	Average Copy Number A	Average Copy Number B	Copy Number Range A	Copy Number Range B
0.1	8	6	4-20. . .	

DETDESC:

DETD(94)

The **DHFR**.sup.- CHO cells described in Example 1 were also used for this example. The non-selective and primary selection media are the. . .

DETDESC:

DETD(96)

The . . . poly A addition site and 3'-genomic flanking sequence are SV40 splice and polyadenylation sites. This vector also contains the murine **DHFR** gene, derived from cDNA. The **DHFR** gene is expressed from the SV40 early promoter and is followed by SV40 splice and polyadenylation signals. The **DHFR** and MIS genes are expressed in opposite orientations. Between the two SV40 poly A sites is a

transcriptional termination element.. . . (see Sato et al., supra). This terminator element is employed in order to block transcriptional interference between the MIS and **DHFR** genes. The pJOD-10 vector also contains the ampicillin-resistance gene and the ColE1 bacteria origin of replication derived from pBR327, allowing. . .

DETDESC:

DETD(97)

Vector . . . constructed (see FIG. 2) from DNA of three origins: (1) vector pD1 (which comprises the human MIS gene); (2) vector pSV2-**DHFR** (which comprises the murine **DHFR** gene); and (3) synthetic oligonucleotide homologous to the human gastrin gene transcriptional terminator. The construction of pD1 is described in Cate et al., European patent application 221,761. The construction of vector pSV2-**DHFR** is described in Subramani et al., supra and is available from the American Type Culture Collection (ATCC 37146).

DETDESC:

DETD(99)

Vector pSV2-**DHFR** was cut with EcoRI and ApaI and the large fragment was gel purified. The double stranded term insert was then ligated into the ApaI/EcoRI pSV2-**DHFR** fragment, forming vector pDT4. Vector pDT4 was cut with AatII and XhoI and the large fragment was ge purified. Vector. . .

DETDESC:

DETD(103)

Approximately 2.times.10.sup.7 **DHFR**.sup.- CHO cells were electroporated as described in Example 1 with a mixture consisting of 200 .mu.g vector pJOD-10 and 200. . . medium. The cells were cultured in this primary selection medium for four days. As in Example 1, approximately 15-30% of **DHFR**- CHO cells survived primary selection. Cells surviving primary selection were seeded into .alpha..sup.- medium supplemented with 0.5 .mu.M MTX (the. . .

DETDESC:

DETD(113)

The MIS gene copy number of the twelve clones was determined analogously to the procedure followed in Example 1 for **DHFR** copy number, with the following modifications. In preparation for electrophoresis, nucleic acid isolated from the cells of this example was. . .

DETDESC:

DETD(121)

Protective (**DHFR**) and product (MIS) genes were supplied by vector pJOD-10 (see FIG. 2). Vector pJOD-10 is described in Example 2. Vector.

. .

DETDESC:

DETD(123)

The protocol for production of NIH/3T3 cells (a **DHFR**.sup.+ cell line) with high copy number integrated foreign DNA was the same as that followed in Example 1 for **DHFR**.sup.- CHO cells except for the changes noted below.

US PAT NO: 4,916,073 L10: 6 of 8

DRAWING DESC:

DRWD(5)

FIG. 4 illustrates the construction of the mammalian cell expression vector pHAGF-MT-**DHFR**.

DETDESC:

DETD(24)

Cloned . . . cells along with the gene of interest. Preferred selectable markers include genes that confer resistance to drugs, such an neomycin, **hygromycin**, and methotrexate. Selectable markers may be introduced into the cell on a separate plasmid at the same time as the. . .

DETDESC:

DETD(43)

For expressing angiogenin in transfected mammalian cells, expression vector pHAGF-MT-**DHFR**, comprising the angiogenin genomic coding sequence (HAGF), the mouse metallothionein-1 (MT-1) promoter, and a **DHFR** selectable marker joined to the SV40 promoter, was constructed.

DETDESC:

DETD(45)

The . . . Hemostasis 54: 282, 1985), comprising the mouse metallothionein (MT-1) promoter, human Factor IX coding sequence, SV40 promoter, and a modified **DHFR** gene (Levinson et al., EPO publication 117,060) was digested with BamHI and EcoRI (FIG. 4). The fragment comprising the pUC13 sequence and the SV40-**DHFR** expression unit was gel purified. This fragment was then joined to the BamHI-EcoRI HAGF fragment. The resultant vector was designated pHAGF-MT-**DHFR** (FIG. 4).

DETDESC:

DETD(46)

Plasmid pHAGF-MT-**DHFR** was then transferred into baby hamster kidney

(BHK) cells by standard calcium phosphate-mediated transfection procedures. Cells containing the vector were. . .

US PAT NO: 4,784,949 L10: 7 of 8

SUMMARY:

BSUM(6)

Selectable . . . synthesis and thus permits the growth of mutant (tk.sup.-) organisms otherwise deficient in it; a sequence which encodes dihydrofolate reductase (**DHFR**) which permits growth in **DHFR** deficient strains; and xanthine-guanosine ribosyl transferase (XGRT), which similarly replaces a deficiency in this enzyme. Such markers were employed in. . .

SUMMARY:

BSUM(13)

Fraley, . . . Jan. 6, 1983, discloses expression of both the gene encoding APH-I and that encoding a protein which confers resistance to **hygromycin** B under the control of an SV40 promoter. Expression was achieved both in yeast and in mammalian mouse Ltk- cells.

DETDESC:

DETD(3)

As . . . These functional characteristics include inactivating a series of antibiotics, and APH-I is distinguishable from APH-II and from the enzyme inactivating **hygromycin** B by virtue of the spectrum of activities it exhibits. Thus, although termed the "Kan gene" herein for brevity and. . .

US PAT NO: 4,721,672 [IMAGE AVAILABLE- L10: 8 of 8

DRAWING DESC:

DRWD(5)

FIG. 4 illustrates the construction of the mammalian cell expression vector pHAGF-MT-**DHFR**.

DETDESC:

DETD(24)

Cloned . . . cells along with the gene of interest. Preferred selectable markers include genes that confer resistance to drugs, such as neomycin, **hygromycin**, and methotrexate. Selectable markers may be introduced into the cell on a separate plasmid at the same time as the. . .

DETDESC:

DETD(43)

For expressing angiogenin in transfected mammalian cells, expression vector pHAGF-MT-**DHFR**, comprising the angiogenin genomic coding sequence (HAGF), the mouse metallothionein-1 (MT-1) promoter, and a **DHFR** selectable marker joined to the SV40 promoter, was constructed.

DETDESC:

DETD(45)

The . . . Hemostasis 54: 282, 1985), comprising the mouse metallothionein (MT-1) promoter, human Factor IX coding sequence, SV40 promoter, and a modified **DHFR** gene (Levinson et al., EPO publication 117,060) was digested with BamHI and EcoRI (FIG. 4). The fragment comprising the pUC13 sequence and the SV40-**DHFR** expression unit was gel purified. This segment was then joined to the BamHI-EcoRI HAGF fragment. The resultant vector was designated pHAGF-MT-**DHFR** (FIG. 4).

DETDESC:

DETD(46)

Plasmid pHAGF-MT-**DHFR** was then transferred into baby hamster kidney (BHK) cells by standard calcium phosphate-mediated transfection procedures. Cells containing the vector were. . .

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  *                  W E L C O M E   T O   T H E                  *
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  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

=> s homologous(w)recombination
          3587 HOMOLOGOUS
          6125 RECOMBINATION
L1          75 HOMOLOGOUS(W)RECOMBINATION

=> s l1 and amplifiable(w)gene?
            58 AMPLIFIABLE
        819284 GENE?
            10 AMPLIFIABLE(W)GENE?
L2           0 L1 AND AMPLIFIABLE(W)GENE?

=> s l1 and amplifi?(4w)gene?
        150806 AMPLIFI?
        819284 GENE?
          9382 AMPLIFI?(4W)GENE?
L3           7 L1 AND AMPLIFI?(4W)GENE?

=>  s l3 and selectable(w)marker?
         21797 SELECTABLE
         16240 MARKER?
           284 SELECTABLE(W)MARKER?
L4           4 L3 AND SELECTABLE(W)MARKER?

=> d l4 1-4 cit,ab

1.  5,030,576, Jul. 9, 1991, Receptors for efficient determination of
ligands and their antagonists or agonists; Thomas J. Dull, et al.,
435/69.7, 69.1; 530/350, 387; 536/27

US PAT NO:     5,030,576                              L4: 1 of 4

ABSTRACT:
Hybrid receptors are provided that comprise (a) the ligand binding domain
of a predetermined receptor and (b) a heterologous reporter polypeptide.
The hybrid receptors are useful for convenient and large scale assay of
biologically active ligands or their antagonists or agonists.

2.  4,997,757, Mar. 5, 1991, Process for detecting potential carcinogens;
Robert H. Schiestl, 435/172.1, 6, 29, 172.3; 935/76, 78, 79, 84 [IMAGE
AVAILABLE]

US PAT NO:     4,997,757 [IMAGE AVAILABLE]            L4: 2 of 4

ABSTRACT:
There is provided a process for screening an agent in order to determine
whether such agent increases the frequency of genome rearrangement in
living matter.
In the first step of this process, there is provided a viable species of
```

Saccharomyces cerevisiae yeast which comprises repeated genetic elements in its haploid genome. These repeated genetic elements are selected from the group consisting of functional and non-functional genetic elements; and these elements are sufficiently homologous so that, under ambient conditions, they recombine with each other and give rise to an indentifiable genome rearrangement which is a deletion.
In the second step of this process, the viable species of yeast is exposed to the agent to be tested. Thereafter, it is plated onto a growth medium which, after the exposed yeast species grows upon it, facilitates the identification of those yeast which have undergone said genome rearrangement.
In the last step of the process, the extent to which the exposed species of yeast has undergone genome rearrangement is determined.
Also disclosed is a the viable yeast strain used in said process, the plasmid used to construct said strain, and a process for constructing said strain.

3. 4,866,042, Sep. 12, 1989, Method for the delivery of genetic material across the blood brain barrier; Edward A. Neuwelt, 514/44; 435/91, 172.2; 935/52, 53

US PAT NO: 4,866,042 L4: 3 of 4

ABSTRACT:
A method for treating genetic and acquired brain disorders is disclosed in which genetic material is introduced into the blood stream for delivery to the brain. Prior to delivery, the interendothelial structure of the BBB is chemically altered to permit passage of the genetic material therethrough. This is accomplished through osmotic disruption of the BBB by administration

This invention was made with Government support under a grant from the Veterans Administration. The Government has certain rights in this invention.

4. 4,859,609, Aug. 22, 1989, Novel receptors for efficient determination of ligands and their antagonists or agonists; Thomas J. Dull, et al., 436/501; 435/7.22, 7.31, 7.9, 968; 436/63, 503, 537; 530/402, 806, 808; 935/81, 109

US PAT NO: 4,859,609 L4: 4 of 4

ABSTRACT:
Hybrid receptors are provided that comprise (a) the ligand binding domain of a predetermined receptor and (b) a heterologous reporter polypeptide. The hybrid receptors are useful for convenient and large scale assay of biologically active ligands or their antagonists or agonists.

```
=> s primary(w)transfectant?
        278164 PRIMARY
            44 TRANSFECTANT?
L5           2 PRIMARY(W)TRANSFECTANT?

=> s l5 and secondary(w)transfectant?
        150365 SECONDARY
            44 TRANSFECTANT?
```

```
             2 SECONDARY(W)TRANSFECTANT?
L6           1 L5 AND SECONDARY(W)TRANSFECTANT?

=> d l6 cit,ab

1.  4,652,522, Mar. 24, 1987, Continuous lymphocyte cell lines, their
production and use; Roger H. Kennett, et al., 435/69.6, 172.1, 240.27,
948; 935/52

US PAT NO:      4,652,522                                  L6: 1 of 1

ABSTRACT:
A method for producing continuous B lymphocyte cell lines and monoclonal
antibodies by such lines is provided. DNA isolated from neoplastic cells
is introduced into stimulated lymphocytes. Individual cells that have
been transformed by the added DNA and that produce antibodies are
clonally expanded. Cultures of these continuous cells are employed to
produce monoclonal antibodies.

=> e skoultchi, arthur I./in
E1            1     SKOUG, PAUL G/IN
E2            1     SKOUGH, EVERT B/IN
E3            0 --> SKOULTCHI, ARTHUR I/IN
E4            2     SKOULTCHI, MARTIN/IN
E5           13     SKOULTCHI, MARTIN M/IN
E6            1     SKOUMAL, DONALD E/IN
E7            2     SKOUPI, DIETER/IN
E8            1     SKOURAS, NICOS P/IN
E9            3     SKOURES, ALEXANDER E/IN
E10           1     SKOUSEN, MARTIN KRABBE/IN
E11           1     SKOUSEN, ORVAL N/IN
E12           1     SKOUSEN, RUSSELL K/IN

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